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American Journal of Diseases of Children

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STUDIES OF INFANT FEEDING. XI

HIGH PROTEIN FEEDING VERSUS HIGH CALCIUM ABSORPTION AS THE CAUSE OF THE INCREASE IN BODY TEMPERATURE OF INFANTS *

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INTRODUCTION

We have found the excessive calcium content of cow's milk to be a disturbing factor in many of the so-called cases of malnutrition and, as any high protein food made under ordinary conditions from cow's milk will of necessity have the greater part of the protein present as calcium caseinate, it seems to us that although protein was the apparent cause of the toxic condition resulting from the feeding to infants of a high protein milk, the real cause might be due to the calcium chemically combined in the calcium caseinate.

We have also found that the feeding to infants of large amounts of pure protein (ash-free paracasin) does not produce any unfavorable symptoms even when the protein is fed with an extremely small amount of whey.[1] As this finding may seem to be contrary to the observations of others we have continued our investigation in an endeavor to find the factor responsible for this difference.

Our investigations have shown that the reduction of the intake of inorganic salts to a point at which chlorin-free urine is eliminated resulted in a febrile condition only when large amounts of calcium was fed as calcium caseinate. We explain these observations as follows:

Under normal conditions sodium can be excreted by the kidneys as chlorid, phosphate, carbonate or sulphate while calcium can be excreted only as chlorid or acid phosphate, the phosphate being only sparingly soluble. A reduction in the intake of chlorin or phosphorus, that is to say, a reduction in the intake of whey, will not interfere with the excretion of sodium because it can form a soluble carbonate, but under the same conditions the excretion of calcium is seriously

* Submitted for publication July 12, 1918.

* From the Boston Floating Hospital Laboratories.

* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

1. Bosworth, A. W., and Bowditch, H. I., and Ragle, B. H.: Casein in Infant Feeding, Am. Jour. Dis. Child., 1914, 8, 120.

interfered with and results in an accumulation or retention of calcium until a toxic condition is finally reached which results in a febrile condition accompanied by the excretion of large amounts of calcium lactate in the urine. This excretion of calcium relieves conditions temporarily, or until the calcium retained again reaches the danger point, when there will follow another fever and an increased elimination of calcium lactate. This condition is relieved by the ingestion of whey which furnishes chlorin for the elimination of the accumulated calcium as calcium chlorid.

A careful scrutiny and analysis of the conditions surrounding the data presented by Holt, Levene, and others,[2] and the data secured by us in some preliminary experiments has led us to investigate the following conditions in infant feeding:

1. The reduction of the intake of inorganic salts to a point which results in the elimination of:

(a) A chlorin-free urine.

(b) A chlorin-free and phosphorus-free urine.

(c) A chlorin-free urine accompanied by the ingestion of large amounts of sodium caseinate.

(d) A chlorin-free urine accompanied by the ingestion of large amounts of available calcium as calcium caseinate.

2. The ingestion of large amounts of calcium caseinate accompanied by the ingestion of large amounts of milk salts.

In presenting the results obtained we have selected the data from one experiment under each of the headings given above.

I. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH A CONTINUED EXCRETION OF CHLORIN-FREE URINE IS PRODUCED

The investigation began with the admission of the baby to the hospital on July 9 and may be divided into six periods as follows:

First Period, 6 p. m., July 9, to 6 p. m., July 12.—From 6 p. m., July 9, until 10 a. m., July 11 (forty hours), the child received only sterile water. From 10 a. m., July 11, to 6 p. m., July 12 (thirty-two hours), the food consisted of a mixture of 840 c.c. of whey, 420 c.c. of breast-milk and 420 c.c. of water and was divided into ten feedings. The child was on the metabolism frame during all three days.

The high output of uric acid, creatinin and creatin during the fast indicates a high endogenous metabolism and is followed by a higher excretion of these substances on the administration of food; the excretion of nitrogen, however, is lowered during the first day following the fast, indicative of a replacement of the nitrogen lost during the endogenous metabolism of the fast. During the fast the chlorin excreted was very small in amount, and both indican and acetone were detected in the urine. The child also had an acetone breath.

2. Holt, L. E., Levene, P. A., and others: The Influence of High Protein Feeding on the General Metabolism, Am. Jour. Dis. Child., 1912, **4**, 265.

Second Period, 6 p. m., July 12, to 6 p. m., July 22.—A period during which the food was changed several times in order to find a mixture suitable for the child. The child was not on the metabolism frame and no analytical data were secured during this period.

Third Period, 6 p. m., July 22, to 6 p. m., July 26.—The child had recovered from his intestinal trouble and was receiving the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

10 per cent. cream	160 c.c.
Buttermilk	800 c.c.
Sterile water	640 c.c.
Milk-sugar	53 gm.

Seven feedings of 210 c.c. each every twenty-four hours. Approximately 637 calories or 145 calories per kilogram body weight.

As he seemed to be in good condition and gaining in weight on this food, he was placed on the metabolism frame at 6 p. m., July 22. During this period he continued to receive the food indicated above and the urine and feces were collected and examined in order to furnish data representing his normal nitrogen metabolism. During this period the body weight increased 165 gm., an average of 41.2 gm. per twenty-four hours. He was well in every respect.

Fourth Period, 6 p. m., July 26, to 6 p. m., July 29.—The child was not on the frame during this period but received the same food given in the preceding period. No macroscopic or microscopic evidence of fat, carbohydrate or protein indigestion was found.

Fifth Period, 6 p. m., July 29, to 6 p. m., August 7.—The child was again placed on the frame and the food received was made up according to the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

10 per cent. cream	161 c.c.
Sterile water	1,439 c.c.
Lactose	89 gm.
Dry paracasein	25 gm.

Seven feedings of 210 c.c. each per twenty-four hours.

This mixture contained about the same amounts of fat, sugar and protein as the mixture given in the two preceding periods. The amount of protein ingested in twenty-four hours was less than in the case of the food made with buttermilk. This was due to the fact that it was almost impossible to manipulate the feeding-bottles so that all the paracasein was removed with the liquid portion of the food.

The inorganic salts were very much decreased in this mixture. In the preceding periods the mixtures fed contained the salts carried in the 160 c.c. of cream and the 800 c.c. of buttermilk. In the present case all the inorganic salts were derived from the 161 c.c. of 10 per cent. cream. The response to this decrease in the inorganic salt intake is shown in the lower figures obtained during this period for sodium chlorid, phosphates and acidity. The food contained 0.116 gm. of sodium chlorid per twenty-four-hour quantity while the amounts excreted dropped from 0.326 gm. the first day to nothing on the eighth and ninth days, chlorin again appearing on the tenth day (the first day of the sixth period) even with a reduction in the chlorin intake on that day. This small chlorin excretion, zero for two days even, was not accompanied by any signs of physical discomfort.

During this period the body weight increased 120 gm., an average of 13.3 gm. per twenty-four hours.

Sixth Period, 6 p. m., August 7, to 6 p. m., August 14.—From 6 p. m., August 7, and during this period the food given to the child was made accord-

ing to the following formula: Fat, 2 per cent.; sugar, 6 per cent.; protein, 2 per cent.

32 per cent. cream	54 c.c.
Sterile water	1,546 c.c.
Lactose	89 gm.
Dry paracasein	28 gm.

Seven feedings of 210 c.c. each per twenty-four hours.

This decreased the inorganic salts again and made the chlorin intake per twenty-four hours equal to 0.033 gm. of sodium chlorid, and the amounts excreted dropped from 0.148 gm. to 0 gm. on the fifth, sixth and seventh days. The child showed no particular discomfort as a result of this rather prolonged confinement on the metabolism frame, but on account of the loss of body weight it was thought best to discontinue the collection of urine and feces and remove the child from the frame at 6 p. m., August 14.

GENERAL DISCUSSION

In connection with the table which gives the result of our daily examination of the urines, we desire to call attention to the following points:

The acidity of the urines and the amounts of phosphates present decreased with the decrease in the amounts of whey ingested. This was to be expected as all the inorganic phosphates ingested were contained in the whey or cream used to make up the formulas. The amounts of organic phosphorus ingested were practically the same through all the periods.

The elimination of chlorin-free urine for two-day and three-day periods without symptoms of any nature is worthy of note.

A very marked increase in the ammonia output during the sixth period of the experiment is noticeable. During the fifth period the whey in the 161 c.c. of 10 per cent. cream furnished considerable neutral salts of organic acids (citrates, albuminates, etc.), the bases of which could be used to neutralize the acid bodies eliminated in the urine. During the sixth period, however, the intake of such base-carrying substances was much reduced, and sufficient bases were not ingested to neutralize the acid bodies eliminated in the urine. This resulted in an immediate increase in the amount of ammonia in the urine with a corresponding decrease in the urea. For the twenty-four hours ending at 6 p. m., August 7, the urine contained 0.261 gm. of nitrogen present as ammonia, and for the twenty-four-hour period ending at 6 p. m., August 8, the first day of the reduction of the intake of the salts to the lowest figure, the urine contained 0.522 gm. of nitrogen in the form of ammonia, an increase of 100 per cent. in one day.

It will be noticed that only a small part of the ammonia is necessary to neutralize the phosphates. Just what the nature of the acid bodies is we are not able to state. We did not detect the presence of acetone bodies in the urine at any time during this period.

TABLE 1.—Showing Change in Composition of Urine as a Result of Reducing the Intake of Inorganic Salts

Date*	Body Weight, Gm.	Urine											Average N. in Feces, Gm.
		Volume, C.c.	Specific Gravity	Total Acid, N/10, C.c.	P_2O_5, Gm.	Cl as NaCl, Gm.	Total N, Gm.	N as NH_3, Gm.	N as Urea, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	
7/10†‡	4,500	505	1.007	82.8	0.577	0.024	1.513	0.161	1.111	0.107	0.030	0.041	.....
1/11†‡	....	630	1.005	54.2	0.534	0.048	1.658	0.247	1.094	0.131	0.028	0.068	.....
7/12†	4,540	670	1.005	144.7	0.574	0.206	1.294	0.110	0.884	0.243	0.037	0.065	.....
7/12–22													
7/23	4,480	700	1.006	127.4	0.810	0.913	1.372	0.319	0.896	0.065	0.020	0.026	0.365
7/24	. ..	660	1.006	97.7	0.918	0.800	1.774	0.292	1.279	0.057	0.019	0.024	0.365
7/25	....	980	1.006	156.8	1.129	1.180	2.387	0.274	1.949	0.084	0.021	0.030	0.365
7/26	4,645	990	1.007	134.6	1.161	1.509	2.550	0.360	2.051	0.084	0.021	0.034	0.365
7/26–29													
7/30	4,730	1,200	1.004	98.4	0.760	0.326	1.747	0.175	....	0.053	0.022	0.020	0.173
7/31	....	1,220	1.003	41.5	0.386	0.332	1.264	0.164	0.929	0.078	0.022	0.030	0.173
8/ 1	....	1,300	1.002	41.6	0.398	0.140	1.092	0.175	0.845	0.053	0.023	0.020	0.173
8/ 2	....	1,240	1.002	39.7	0.379	0.298	1.146	0.208	0.724	0.066	0.021	0.025	0.173
8/ 3	....	1,070	1.003	42.8	0.317	0.223	1.079	0.216	0.713	0.057	0.019	0.022	.....
8/ 4	....	670	1.003	24.1	0.233	0.115	0.925	0.173	0.522	0.045	0.018	0.021	.....
8/ 5	....	1.170	1.003	56.2	0.370	0.047	1.409	0.216	0.963	0.081	0.020	0.028	.....
8/ 6	....	1.060	1.003	33.9	0.357	0.000	1.676	0.261	....	0.072	0.020	0.029	.....
8/ 7	4,850	1.060	1.003	33.9	0.357	0.000	1.676	0.261	....	0.072	0.020	0.029	.....
8/ 8	....	1.060	1.002	38.2	0.232	0.148	1.039	0.522	0.284	0.072	0.020	0.027	.....
8/ 9	....	850	1.003	47.6	0.390	0.065	1.275	0.509	....	0.084	0.020	0.015	.....
8/10	..	970	1.003	26.6	0.317	0.067	1.249	0.494	....	0.082	0.022	0.019	.....
8/11	....	1,060	1.003	27.6	0.378	0.015	1.276	0.392	0.613	0.086	0.020	0.020	.....
8/12	....	1,000	1.003	32.0	0.275	0.000	1.036	0.476	....	0.087	0.017	0.015	.....
8/13	....	900	1.005	28.8	0.303	0.000	1.411	0.731	....	0.075	0.017	0.019	.....
8/14	4,510	760	1.003	33.4	0.357	0.000	1.105	0.655	0.378	0.092	0.020	0.017	.....

* Twenty-four-hour period ending 6 p. m. † Traces of indican appeared in the urine on these days. ‡ Traces of acetone on these days.

The amounts of creatinin and creatin excreted during the fasting period were much above the normal as would be expected. During the other three periods the creatinin figures are strikingly uniform.

During the third period, when the food contained an excess of all constituents, the child increased in body weight an average of 41.2 gm. per twenty-four hours and the creatin output averaged 0.028 gm. per day. In the fifth period when the whey had been reduced to the amount carried in 161 c.c. of 10 per cent. cream, the average daily increase in body weight was reduced to 13.3 gm. and the average daily creatin excretion was 0.025 gm. In the sixth period there was an average daily decrease in body weight of 48.6 gm., and the average daily excretion of creatin was 0.015 gm. with a daily fluctuation giving figures between 0.027 and 0.015 gm.

No symptoms of any nature developed during the fifth and sixth periods.

II. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH A CONTINUOUS EXCRETION OF CHLORIN-FREE AND PHOSPHORUS-FREE URINE IS PRODUCED

We have shown in a previous paper how the feeding of an excessive amount of calcium may result in the precipitation within the intestines of all the ingested phosphorus as insoluble calcium phosphate and thus reduce the phosphorus metabolism to such a low level that the urine becomes phosphorus-free and contains a large amount of carbon dioxid.[3]

We have been able to take advantage of this fact and, by the feeding of a synthetic food containing no inorganic salts but considerable soluble calcium, we have reduced the chlorin intake and output to nil and brought about the excretion of a phosphorus-free urine.

This investigation began when the child was placed on the metabolism frame, July 13, 1915, and may be divided into two periods.

First Period, 9 a. m., July 13, to 9 a. m., July 14.—During this first twenty-four hours the child received 1,260 c.c. of a modified milk containing 2 per cent. of fat, 6 per cent. of lactose and 2 per cent. of protein.

Second Period, 9 a. m., July 14, to 9 a. m., July 22.—During the next eight days the child received a chlorin-free synthetic[4] milk containing pure butter fat, 2 per cent.; lactose, 6 per cent.; sodium caseinate, 2 per cent., and calcium acetate [$(CH_3COO)_2Ca.H_2O$)] 0.167 per cent. The only phosphorus present in this food was that contained within the casein molecule. The child received 1,260 c.c. of this food every twenty-four hours.

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3. Bowditch, H. I., and Bosworth, A. W.: Boston Med. and Surg. Jour., 1917, **177,** 864.

4. Bowditch, H. I., and Bosworth, A. W.: Studies of Infant Feeding, Tr. Am. Ped. Soc., 1916, **28,** 114.

The data secured will be found in Table 2. By consulting the table it will be noticed that the urine became alkaline on the first day of the second period and remained so while the child received the synthetic milk. All the urines during this period were heavily charged with carbon dioxid, the addition of a drop of hydrochloric acid causing a marked effervescence.

The urine became chlorin-free on the first day of the second period and phosphorus-free on the fourth day. A marked increase in the ammonia excretion is noticed during the time the child received the food containing no milk salts. Most of the phosphoric acid resulting from the digestion of the casein was precipitated in the intestines as insoluble calcium phosphate and appeared as such in the feces. The remainder must have been assimilated and retained, for the urine soon became phosphorus-free.

No symptoms of any kind developed during this experiment.

III. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT WHERE A CONTINUED EXCRETION OF CHLORIN-FREE URINE IS PRODUCED ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF SODIUM CASEINATE

The child selected for this experiment was 11 months old, weighed 7,129 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 9:30 a. m., July 26. The investigation may be divided into two periods.

First Period, July 26, to July 27.—During the first twenty-four hours the child received a food made up as follows:

Whole milk	75 c.c.
Dextri-maltose to make total sugar	5%
Boiled water to make	100 c.c.

Five feedings, 227 c.c. each.

This food contained fat, 3 per cent.; sugar, 5 per cent., and protein 2.4 per cent.

Second Period, July 27 to August 7.—At 9:30 a. m., July 27, the food was changed to a synthetic milk containing fat, 2 per cent.; sugar, 6 per cent., and sodium caseinate, 6.5 per cent. He received five feedings of 227 c.c. each per day. The feces was so small in amount that no work was done on it. (In this connection see a previous paper by us.[5])

The data secured will be found in Table 3. Here we again have an alkaline urine containing large amounts of carbonate and ammonia. The uric acid, creatinin and creatin outputs show no marked variations from day to day. No symptoms of any nature developed.

5. Bowditch, H. I., and Bosworth, A. W.: Boston Med. and Surg. Jour., 1917, **177**, 864.

TABLE 2.—Showing Change in Composition of Urine as a Result of Reducing the Intake of Inorganic Salts to a Point which Results in the Excretion of a Chlorin- and Phosphorus-Free Urine

24-Hour Period Ending 1915	Body Weight, Gm.	Urine									Feces			
		Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	P_2O_5, Gm.	Chlorin, Gm.	Total N Gm.	N as NH_3 Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.	Dry Weight, Gm.	Fat, Gm.	Calcium Oxid, Gm.	Phosphoric Oxid, Gm.
8/14	5,336	510	1.009	113.2	0.816	0.707	1.948	0.251	0.057	None	12.15	5.01	0.937	0.363
8/15	....	260	1.014	Alk.	0.286	None	1.877	0.497	0.058	None	7.67	3.03	0.571	0.186
8/16	....	530	1.008	Alk.	0.133	None	1.677	0.502	0.062	None	7.06	1.88	0.660	0.131
8/17	....	410	1.009	Alk.	0.082	None	1.484	0.786	0.048	None	7.47	3.07	0.573	0.126
8/18	....	300	1.012	Alk.	0.054	None	1.490	0.572	0.045	None	9.28	3.04	0.904	0.213
8/19	....	300	1.011	Alk.	None	None	1.374	0.539	0.030	None	3.58	0.87	0.243	0.084
8/20	....	240	1.010	Alk.	None	None	1.291	0.304	0.040	None	6.68	2.55	0.565	0.175
8/21	....	480	1.007	Alk.	None	None	1.032	0.454	0.046	None	6.50	2.41	0.612	0.150
8/22	4,768	420	1.006	Alk.	None	None	0.997	0.316	0.041	None	5.27	2.46	0.457	0.128

TABLE 3.—Showing Change in Composition of Urine as a Result of Reducing the Intake of Inorganic Salts and Feeding Large Amounts of Sodium Caseinate

24-Hour Period Ending	Body Weight, Gm.	Urine											
		Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	Phosphorl. Oxid, Gm.	Total N, Gm.	N as NH₃ Gm.	Uric Acid, Gm.	Creatinin, Gm	Creatin, Gm	Calcium Oxid, Gm.	Lactic Acid, Gm.
7/27	7,129	640	1.008	83.2	0.672	0.826	2.87	0.39	0.147	0.078	0.089	0.029	None
7/28	....	760	1.010	Alk.	0.399	0.456	4.36	0.85	0.120	0.074	0.075	0.056	None
7/29	....	780	1.011	Alk.	0.137	0.741	5.13	2.88	0.110	0.078	0.020	0.055	None
7/30	..	830	1.011	Alk.	0.145	0.315	6.51	0.49	0.089	0.078	0.050	0.076	None
7/31	....	810	1.011	Alk.	0.062	0.194	5.90	0.41	0.092	0.071	0.050	0.060	None
8/1	...	840	1.013	Alk.	0.047	0.378	6.88	0.85	0.120	0.080	0.065	0.077	None
8/2	...	840	1.010	Alk.	0.082	0.294	8.47	0.85	0.073	0.074	0.074	0.097	None
8/3	....	1,020	1.010	Alk.	0.002	0.306	7.14	1.26	0.119	0.077	0.072	0.135	None
8/4	....	840	1.010	Alk.	0.000	0.327	8.88	2.42	0.092	0.069	0.060	0.068	None
8/5	....	760	1.013	Alk.	0.000	0.800	7.02	3.02	0.076	0.066	0.048	0.041	None
8/6	....	570	1.013	Alk.	0.000	0.500	8.06	3.17	0.084	0.072	0.050	0.031	None
8/7	7,013	680	1.011	Alk.	0.000	0.200	8.85	2.53	0.107	0.081	0.070	0.064	None

IV. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH CHLORIN-FREE URINE IS EXCRETED, ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF CALCIUM CASEINATE

The child selected was 10 months old, weighed 5,477 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 8 p. m., July 11. The investigation may be divided into two periods.

First Period, July 11 to July 12.—During the first twenty-four hours the child received a food made up as follows:

Fat-free milk	75 c.c.
Dextri-maltose	5 gm.
Boiled water to make	100 c.c.

Six feedings, 170 c.c. each.

This food contained fat, a trace; sugar, 8 per cent., and protein 2.4 per cent.

Second Period, July 12 to July 18.—At 8 p. m., July 12, the food was changed to one made according to the following formula:

32 per cent. cream	65 c.c.
20 per cent. lactose solution	377 c.c.
Calcium caseinate	87 gm.
Sodium citrate	80 grains
Water to make	1,392 c.c.

Six feedings, 170 c.c. each.

This food contained fat, 1.50 per cent.; sugar, 5.63 per cent.; protein, 6.25 per cent., and calcium oxid, 0.1575 per cent. The data secured during this experiment will be found in Table 4 and Chart 1. The food used for this investigation had a low chlorin and high calcium content.

The most striking point brought out by the data in Table 4 is the appearance of lactic acid in the urine on the 15th, followed by a toxic condition which manifested itself during the night of the 16th. The appearance of the lactic acid is accompanied by a greatly increased elimination of calcium. It will be noticed that the temperature of 102.4 F. recorded on the morning of the 17th is reduced during the day and seemed to be directly associated with the ingestion of the early morning feeding. Possibly the lactose in the food had some influence in reducing the temperature.

The lactic acid was determined by extracting the acidulated urine with ether, distilling off the ether, dissolving the residue in water, evaporating to a thick syrup, taking up with water, converting the lactic acid to the zinc salt by the addition of zinc oxid, boiling, filtering, evaporating the filtrate to dryness, drying in the oven for two hours and weighing. The weights were checked by burning the zinc lactate and weighing the residual zinc oxid. The lactic acid was identified by the crystals of zinc lactate.

Owing to the uncomfortable condition of the child, he was removed from the metabolism frame on the 18th, but continued to receive the

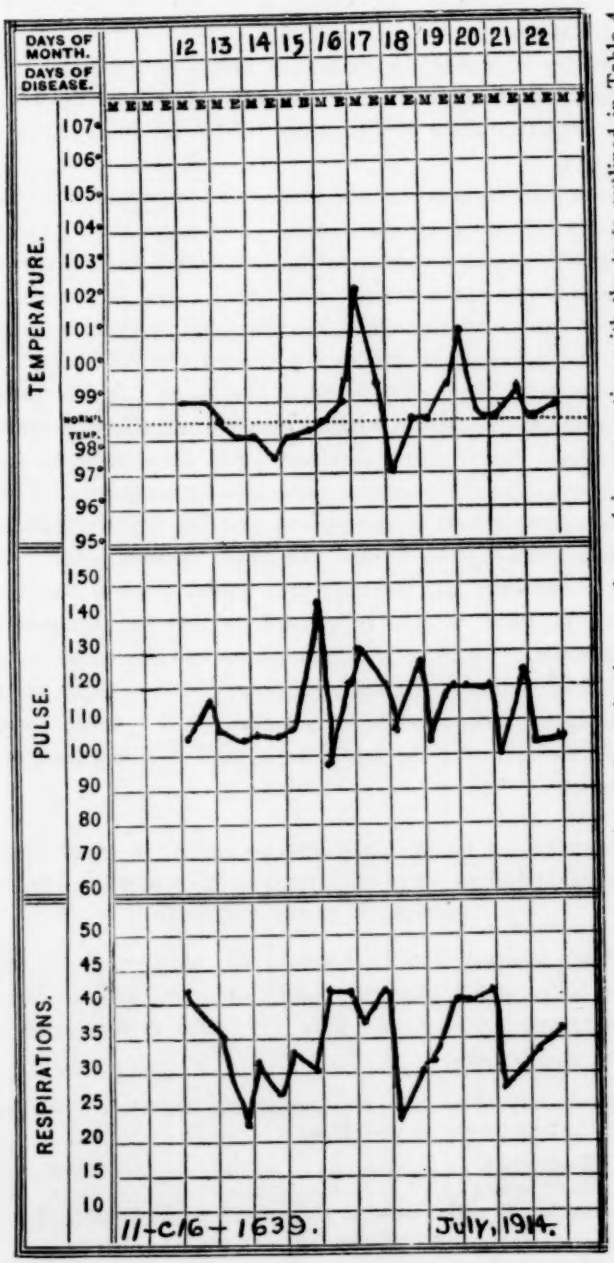

Chart 1.—Record of the temperature, pulse and respiration as observed in connection with the tests outlined in Table 4.

same food until the morning of the 21st. During the night of the 19th another temperature was noticed which also seemed to be lowered by the ingestion of food.

The greatly increased elimination of uric acid, creatinin and creatin during this experiment is to be expected as a result of the fever. It is worthy of note that none of the urines in this set showed the presence of carbonates.

The toxic condition produced during this experiment we believe to be due to the following circumstances. The digestion of fat and protein within the intestine results in the production of acids, fatty acids from fat and amino-acids or polypeptic acids from the proteins. These acids do not remain as free acids but immediately unite with the bases present in the intestines to form salts, the soluble salts being absorbed, the insoluble salts being eliminated in the feces. In the presence of the large amount of calcium carried into the intestines in combination with the casein many more of these acids form calcium salts than would be the condition under more normal circumstances. The soluble organic salts are carried to the tissues and the organic part used for vital activities leaving as refuse the base calcium which has acted simply as a conveyor and neutralizer. Under normal conditions this calcium would form chlorid or phosphate and be eliminated in the urine immediately. Under the conditions of this experiment there was no chlorin available for such purpose and very little phosphorus. The result is an accumulation of calcium until a toxic condition is reached and then, during the fever, an abundant elimination of soluble calcium lactate.

V. THE FEEDING OF LARGE AMOUNTS OF CALCIUM CASEINATE WHEN ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF INORGANIC SALTS (WHEY)

The child selected was 5 months old, weighed 5,371 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 8 p. m., July 11. The investigation may be divided into two periods.

First Period, July 11 to July 12.—During the first twenty-four hours the child received a food made up as follows:

Whole milk	60 c.c.
Boiled water	40 c.c.
Maltose to make sugar	6%

Six feedings, 170 c.c. each.

This food contained, fat, 2.4 per cent.; sugar, 6 per cent., and protein 1.9 per cent.

TABLE 4.—Showing Change in Composition of Urine as a Result of Reducing the Intake of Inorganic Salts and Feeding Large Amounts of Calcium Caseinate

24-Hour Period Ending at 8 p. m., 1914	Urine												Feces			
	Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	P_2O_5, Gm.	Total Nitrogen, Gm.	Nitrogen, as Ammonia, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.	Dry Weight, Gm.	Total N, Gm.	P_2O_5, Gm.	Calcium Oxid, Gm.
7/12	660	1.010	59.4	0.809	0.53	3.53	0.340	0.145	0.086	0.034	0.0462	0.0000	10.1	0.606	0.170	1.075
7/13	720	1.009	13.0	0.655	0.36	4.29	0.363	0.092	0.060	0.049	0.0432	0.0000	9.1	0.528	0.122	0.901
7/14	750	1.010	123.0*	0.394	0.34	4.83	0.522	0.085	0.072	0.023	0.0825	0.0000	9.0	0.653	0.109	0.603
7/15	626	1.011	82.2*	0.031	0.95	4.62	1.403	0.186	0.097	0.052	0.1640	0.2799	13.0	0.868	0.222	0.902
7/16	680	1.013	21.8*	0.000	0.20	5.21	0.823	0.336	0.113	0.127	0.1537	0.5208	14.0	0.963	0.252	1.244
7/17	650	1.016	27.3	0.073	0.31	6.64	0.454	0.325	0.100	0.100	0.1274	0.3608	14.5	0.931	0.246	0.940
7/18	730	1.015	2.9	0.000	0.22	6.95	1.083	0.380	0.123	0.083	0.2015	0.5075	....	....	....	....

* Alkalinity.

TABLE 5.—Showing Composition of the Urine when Large Amounts of Calcium Caseinate is Ingested Accompanied by Large Amounts of Inorganic Salts (Whey)

24-Hour Period Ending at 8 p. m., 1914	Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	P_2O_5, Gm.	Total Nitrogen, Gm.	Nitrogen as Ammonia, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.
7/12	600	1.010	30.0	0.714	0.68	2.50	0.285	0.107	0.071	0.042	0.0132	0
7/13	620	1.010	20.0*	0.608	0.59	2.97	0.576	0.099	0.071	0.045	0.0372	0
7/14	580	1.013	93.0*	0.304	0.33	4.93	0.601	0.085	0.070	0.054	0.0152	0
7/15	670	1.014	60.0*	0.304	0.37	5.07	0.657	0.107	0.070	0.065	0.0938	0
7/16	740	1.013	59.0*	0.622	0.31	8.88	0.315	0.096	0.072	0.073	0.1154	0
7/17	670	1.014	36.0*	0.539	0.35	8.85	0.555	0.103	0.074	0.052	0.1072	0
7/18	730	1.015	48.0*	1.613	0.45	8.47	0.220	0.100	0.073	0.050	0.0847	0

* Alkalinity.

Second Period, July 12 to July 18.—At 8 p. m., July 12, the food was changed to one made according to the following formula:

32 per cent. cream	65 c.c.
20 per cent. lactose solution	331 c.c.
Calcium caseinate	87 gm.
Sodium citrate	80 grains
Whey	580 c.c.
Water to make	1,392 c.c.

Six feedings, 170 c.c. each.

This food contained, fat, 1.50 per cent.; sugar, 6.4 per cent., and calcium oxid, 0.1575 per cent.

The data secured will be found in Table 5. In this case sufficient chlorin and phosphorus had been ingested to permit the elimination of all the calcium as soluble chlorid or phosphate, and our data shows nothing worthy of note, the ingestion of the large amount of calcium causing no upset in the condition of the child.

CONCLUSIONS

We have shown that the ingestion of large amounts of calcium and the absorption of this calcium as organic salts, if not accompanied by the ingestion of sufficient chlorin or phosphorus to permit of the formation of soluble salts will result in an accumulation of calcium in the tissues which is followed by a toxic condition and the elimination of calcium lactate in the urine.

The toxic condition noticed by others when a high protein synthetic food was fed was probably the result of the high calcium content of the food, as our work reported in this and previous papers seems to indicate, and not the result of the high protein content, the protein being responsible only to the extent that it is the carrier of the calcium in the form of calcium caseinate.

Whether the toxic condition noticed is the result of the accumulated calcium itself or to a calcium salt, possibly calcium oxalate, we are not prepared to state.

C. Bruger[6] has recorded the fact that the injection of neutral or alkaline phosphates of sodium resulted in a diminution in the calcium content of the serum and a condition of tetany. In view of the fact that the overloading of the serum with neutral or alkaline phosphates would favor the precipitation of calcium salts we are inclined to believe our results and his to be manifestations of the same phenomenon.

We also believe the observations of Marriott and Howland,[7] in which they noticed a diminution in the calcium content of the serum and a marked phosphorus retention, to have some bearing on the same phenomenon.

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6. Bruger, C.: Toxicity of Phosphates in Relation to Blood Calcium and Tetany, Jour. Pharmacol., 1917, **10,** 105.

7. Marriott, W. McK., and Howland, John: Phosphate Retention as a Factor in the Production of Acidosis in Nephritis, Arch. Int. Med., 1916, **18,** 108.

THE EFFECT OF ALKALI AND MALT PREPARATIONS ON THE RETENTION OF CALCIUM IN INFANCY*

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There is no paucity of literature concerning the metabolism of calcium in infancy, but very little is known regarding the factors that may influence it; even the effect of the organic ingredients of milk, with the exception of fat, has been very little studied, and there are many facts regarding the influence of fat that are not entirely clear. There is a still greater gap in our knowledge with regard to the effect of inorganic compounds on calcium metabolism. How calcium salts themselves act on the retention of calcium has been studied to a certain extent, it is true, but as to the influence of other salts, our knowledge remains very meager.

THE EFFECTS OF ALKALI

Dugois and Stolte[1] were the first to study the effect of alkali on calcium retention in infancy. They attribute the favorable effect of Keller's malt soup on calcium retention to the alkali contained in it. In an endeavor to prove this they made observations on two children in six periods. They believed that they showed a favorable influence of the alkali on calcium retention. Their results, however, were so very irregular, that it is hard to accept them as conclusive. For instance, in one experiment there was a very distinct loss of calcium in the control period and only a slight retention in the period with alkali. The difference in the calcium balance between the two periods was very great but was due not so much to satisfactory retention in the alkali period as to a very marked loss in the control period. The other two experiments were not very impressive, the difference being very slight in the amount of calcium retained. To explain their peculiar results they maintain that "the smaller the balance of calcium was at first, the greater became the increase of calcium retention." The explanation that they offer that every increase of alkali contributes to neutralize the acids produced in metabolism, thus saving the body calcium, does not seem very likely. Calcium plays a very small part in the neutralization of the ordinary acids of metabolism and ammonia would be much more readily available than would calcium.

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* Submitted for publication July 10, 1918.

* From the Harriet Lane Home and from the Department of Pediatrics, Johns Hopkins University.

1. Dubois, M., and Stolte, K.: Jahrb. f. Kinderh., 1913, **77**, 21.

In the case of adults, Rumpf[2] found an increase of calcium excretion of 50 per cent. when sodium lactate and lactic acid were given, while Lunin demonstrated that sodium carbonate would diminish the excretion of calcium in the stool. Rumpf found the same with sodium phosphate and sodium sulphate.

Recently Givens and Mendel[3] have made animal experiments in which they not only failed to find any favorable effects of alkali, but, on the contrary, obtained a rather unfavorable effect on calcium retention, though they concluded reservedly that the administration of base produced no significant effect on the calcium balance in the dog. There is the possibility that if young animals had been used, the results might have been different, but this is only a conjecture.

AUTHOR'S EXPERIMENTS

I wished to determine on the same child and with the same malt preparation whether the beneficial effect on the calcium retention attributed to malt extracts is due to the extract itself or to the added alkali. For this reason I used a liquid malt preparation (maltine plain) which contained by analysis from 50 to 54 per cent. maltose and from 1.3 to 1.5 per cent. dextrine, expressed as glucose, containing no additional alkali. During certain periods alkali in the form of sodium bicarbonate was added.

The child used for the observations was a vigorous but not very well nourished infant of fourteen months. There was no recognizable disease and no evidence of rickets. Except for a mild attack of bronchitis, at which time the experiment was interrupted, he remained well throughout the whole period of observation.

Experimental periods for calcium metabolism should be as long as possible. The duration of each period was four days. Short periods are unsatisfactory for the study of calcium metabolism. The stools contain a large amount of calcium. The longer the period, the less the influence of incomplete stool collection. At the beginning of each fore-period, the diet for each entire period was made up at one time, sterilized and preserved on ice. The analysis of the food was made in triplicate. The interval between the periods was at least three days. The infant was put on the special diet for each period for two days before the collection of specimens was begun. The infant was on a special metabolism bed. The collection of urine and feces was completely satisfactory throughout the experiment.

Calcium was determined by McCrudden's method, nitrogen by the method of Folin and Farmer, fat by the Babcock apparatus and

2. Cited by O. Rommel., Arch. f. Kinderh., 1903, **37,** 261.
3. Givens and Mendel: Jour. Biol. Chem., 1917, **31,** 427.

TABLE 1.—RESULTS OF EXPERIMENTS TO DETERMINE THE CALCIUM RETENTION IN A 14 MONTHS' OLD CHILD

Period	Food (per Diem)						Stools		Body Weight		Calcium (as CaO) per Diem			
	Whole Milk				Alkali* ($NaHCO_3$)	Maltine Plain	Number During Period	Consistency	Before and After the Period, Gm.	Difference, Gm.	Intake	Output		Retention
	Protein, %	Fat, %	Sugar, %	Amount								Urine	Stool	
I	2.2	2.6	5.0	213 c.c. ×5	.....	.....	7	Mostly formed	8,000 7,900	−100	2.151	0.054	1.932	+0.165
												1.986		
II	2.5	3.5	4.8	213 c.c. ×5	4% solution (10 c.c. × 5) = 2 gm. per day	.....	8	Mostly formed	7,630 7,660	+30	1.891	0.037	1.693	+0.161
												1.730		
III	2.3	2.8	5.0	213 c.c. ×5	.....	.....	11	Formed	7,660 7,760	+100	2.049	0.046	1.715	+0.288
												1.761		
IV	2.2	2.8	4.9	213 c.c. ×5	6% solution (10 c.c. × 5) = 3 gm. per day	.....	12	2 hard 2 soft 8 formed	8,035 8,005	−30	1.968	0.019	1.874	+0.075
												1.893		
V	2.5	2.8	5.2	213 c.c. ×5	.....	11 c.c. × 5	6	All pasty	8,300 8,310	+10	2.124	0.041	1.476	+0.607
												1.517		
VI	2.4	3.2	5.0	213 c.c. ×5	6% solution (10 c.c. × 5) = 3 gm. per day	11 c.c. × 5	12	Mostly formed	8,500 8,515	+15	2.115	0.024	2.276	−0.187
												2.302		
VII	2.1	2.6	6.4	213 c.c. ×5	.....	.....	10	Formed	8,250 8,150	−100	1.994	0.032	1.683	+0.279
												1.715		
VIII	2.5	2.8	4.7	213 c.c. ×5	.....	11 c.c. × 5	13	Formed	8,175 8,270	+95	2.201	0.030	1.842	+0.329
												1.872		

* Alkali solutions were kept separately and mixed with the food just before feeding.

carbohydrate by Shimidzu's[4] method. The analytic results are given in Table 1. They are calculated on a twenty-four hour basis.

Table 1 shows that there was some variation in the amount of the organic ingredients as well as calcium in the specimens of milk. The differences, however, were not great enough to have any possible effect on the retention of calcium, whereas the bicarbonate and maltine added were in amounts large enough to be considered as new factors.

DISCUSSION OF THE RESULTS

If the average results of similar periods are investigated, they will be found to be as summarized in Table 2.

TABLE 2.—SUMMARY OF THE AVERAGE RESULTS OF SIMILAR PERIODS

Additions to Whole Milk	Number of Period	Retention of Calcium (CaO)	
		Absolute, Gm.	Average, Gm.
0	I	+0.165	+0.244
0	III	+0.288	
0	VII	+0.279	
Alkali 2 gm. $NaHCO_3$	II	+0.161	+0.118
3 gm. $NaHCO_3$	IV	+0.075	
Maltine plain	V	+0.607	+0.468
Maltine plain	VIII	+0.329	
Maltine plain and alkali	VI	−0.187	

It is very clear at first sight that the retention of calcium in the average whole milk period is twice as large as that in the average alkali period. The retention was not so bad in Period II, in which alkali was used, especially if it is compared with Period I, but the retention of Period I is the worst in all the three "plain" periods, whereas the amount of alkali used in Period II was smaller than in the other alkali periods. The impression that one receives is that calcium retention becomes worse as the alkali added increases in amount. It is therefore possible to say that it is not through the alkali itself that malt extract acts favorably on calcium storage. The quantity of alkali, in proportion to the amount of whole milk given, that was used by Dubois, Stolte and by myself was approximately the same. They used the equivalent of 34 c.c. of normal alkali per liter of whole milk whilst I used the equivalent of from 24 to 36 c.c. of normal alkali per liter of whole milk. It is necessary to make the basis of comparison on the amount of milk taken as Dubois and Stolte do not give the weight of the two children used for their observations.

4. Shimidzu: Biochem. Ztschr., 1908, **13**, 243.

What, then, if malt extract is used with alkali, as the usual preparation of malt extract contains some alkali? Period VI gives the answer. This is the period in which the calcium balance was negative. Though this experiment with malt extract and alkali was not repeated, yet the results, taken with those of other periods, are conclusive enough to show that there is no favorable effect from the alkali, even when this is combined with a malt preparation.

On the other hand, in the periods in which the malt extract alone was administered, the result was quite definite. The average retention during the two maltine periods was almost twice as great as that during the whole milk periods. The balance was especially good in Period V, in which the infant had only six stools, which were all loose and pasty. In Periods VI and VIII the stools were not noticeably different in number and consistency from those in the other periods, with the exception of Period V. It is thus evident that it is the malt preparation and not the alkali which affects calcium storage favorably. It is true that the usual malt extract preparations used in infant feeding contain alkali but this is usually too small in amount to act as an unfavorable factor. In these experiments may be seen the effects of malt extract alone.

EFFECT OF CARBOHYDRATE ON CALCIUM RETENTION

Strictly speaking there is not a single report of the effect of carbohydrate on calcium which is quite free of criticism. Rothberg[5] and Birk[6] determined the effect of the organic ingredients of milk on the calcium balance. This work, however, was not well planned to demonstrate any effect from the carbohydrates alone because when the fat of the food was increased it was not done without at the same time changing the carbohydrate content of the food. One cannot draw from their experiments any definite conclusions regarding carbohydrates in general, or of malt preparations in particular, nor can we derive any definite information regarding the effect of malt preparations from the work of Arndt[7] or Freund.[8] In an attempt to follow the fate of fat in the intestines of infancy, Usuki[9] found a favorable effect from Keller's malt soup extract on calcium retention. Each infant retained much more calcium when malt extract was used than when simple maltose was used. The question is: To what does malt extract owe this favorable influence, carbohydrate or alkali?

5. Rothberg: Jahrb. f. Kinderh., 1907, **66,** 69.
6. Birk: Jahrb. f. Kinderh., 1907, **66,** 300.
7. Arndt: Inaug. Diss. Breslau, 1901, cited by Rothberg, Jahrb. f. Kinderh., 1907, **66,** 71.
8. Freund: Biochem. Ztschr., 1907, **16,** 471.
9. Usuki: Jahrb. f. Kinderh., 1910, **72,** 42.

Preparations which come under the name of malt extract contain a number of different substances unknown as well as known. It was shown by Usuki that it is not maltose alone which exerts the favorable effect. Our knowledge is still too poor to be able to judge of the effect of a simple carbohydrate, even of lactose itself. There is not sufficient nitrogenous matter in the extract to ever exercise an appreciable influence in either direction. The total nitrogen of our malt extracts was 1.2 and 0.98 gm. in 100 c.c. of the specimens used in Period V and Periods VI and VIII, respectively. There is a small amount of ash in malt extract but in the amounts used in the milk dilutions this is hardly great enough to exert any influence. Thus, one of the chief constituents is phosphoric oxid. My analysis showed that the specimens used in Period V and Periods VI and VIII contained 0.305 and 0.311 gm. of phosphoric oxid in 100 c.c., respectively, or 0.153 and 0.156 gm. in twenty-four hours. This amount is of no consequence when it is considered that milk contains about 0.7 gm. phosphoric oxid in 100 c.c. and from the milk the infant received 7.45 gm. of phosphoric oxid each day.

We cannot discover the substance or substances which alone affect calcium retention favorably, but we can say safely of malt extract that it is not the alkali in it or the alkali added to it which acts beneficially on calcium storage. It is rather the malt extract itself—the malt extract without alkali.

CONCLUSIONS

In a normal infant the addition of alkali to milk produced not only no favorable effect on the retention of calcium but a distinctly unfavorable one.

Malt extract alone without alkali acts beneficially on calcium storage.

If malt soup has a favorable effect on calcium metabolism, it is not as a result of the alkali originally contained in it or added to it.

Malt extract to which a considerable amount of alkali has been added seems to have a rather unfavorable influence on the calcium balance.

THE RELATIVE EFFICIENCY OF THE DIFFERENT MERCURIAL PREPARATIONS IN THE TREATMENT OF CONGENITAL SYPHILIS IN INFANTS AND CHILDREN

AS DETERMINED BY A QUANTITATIVE ANALYSIS OF THE MERCURY ELIMINATED IN THE URINE *

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In spite of the different forms of arsenic used under various trade names, mercury, in some form, still holds the foremost place in the treatment of syphilis. Even when the arsenic preparations are used, mercury is usually continued for long periods in order to effect a cure.

Many of the salts of mercury, including metallic mercury itself, are administered in various ways: by mouth, by insufflation, subcutaneously and by inunction.

ABSORPTION AND ELIMINATION OF MERCURY

Owing to the difficulty in detecting mercury in the body fluids, little light has been thrown on the question as to what extent the different forms of mercury were absorbed and how eliminated. Meyer and Gottleib[1] state, "the excretion of mercury in the urine offers a means of estimating the amounts of mercury circulating in the body and the duration of its action. After absorption it circulates as a compound of mercury albuminate and sodium chlorid. It is chiefly excreted in the feces and only small amounts in the urine, and that the mercury present in the circulation probably maintains a definite ratio to the amount excreted in the urine." "The determination of the curves of elimination of mercury is of importance for the estimation of the value of different methods of administration." [2] Jones[3] states, "mer-

* Submitted for publication July 15, 1918.
* Read at the meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

1. Meyer and Gottleib: Pharmacology, Clinical and Experimental. Philadelphia, J. B. Lippincott Company.
2. Burgi: Arch. f. Dermatol. u. Syph., **79,** 1906.
3. Jones: Brit. Med. Jour., 1888, p. 660.

cury is chiefly eliminated by the urine and when it causes purgation, more is eliminated by the bowel."

Whether mercury by inunction is absorbed by the skin, has long been a cource of controversy. Up to the present year, many of the foremost authorities have claimed that no mercury was absorbed by the skin, but that the mercury was volatilized by means of the body heat and absorbed through the respiratory tract.

Wile and Elliot,[4] by employing a modification of the Reinsch method, were able to detect as small an amount of mercury as 0.025 mg. in 300 c.c. of urine. By using this method they were able to demonstrate that "the mode of absorption of mercury in the inunction cure is both by volatilization and by direct absorption through the skin." Schamberg, Kolmer, Raiziss and Gavron,[5] in an experimental study on rabbits, were able to demonstrate that "the chief avenue of absorption of mercury when applied by inunction is the skin and that rabbits may be fatally poisoned with mercury by inunction, even when no opportunity of absorption through the lungs exists."

LITERATURE ON THIS SUBJECT

So far as we have been able to determine in reviewing the literature, no work has been done on the elimination of mercury in the treatment of syphilis in infants and children.

Up to the present time, the form, dose and method of administration of mercury in the treatment of syphilis in infants and children have been more or less haphazard. Almost all of the modes are in vogue, the physician using the method which seems in his hands, to produce the best clinical results or, frequently, the one which may be given with the least suspicion as to what is being given.

Whatever form of mercury is administered, the object has been to produce a disappearance of the symptoms of syphilis and maintain the mercurial dosage in such quantities, for long periods of time, as to keep within the tolerance as indicated by salivation and diarrhea. That mercury, even by inunction in sufficient doses, is toxic to rabbits was shown in the experiments by Schamberg and his associates.[5] In these experiments five rabbits were given from two to four inunctions of calomel ointment or mercury ointment. All of the rabbits died and showed acute hyperemia of the glomeruli and cloudy swelling of the parenchyma.

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4. Wile and Elliot: Mode of Absorption of Mercury in the Inunction Treatment of Syphilis, Jour. Am. Med. Assn., 1917, **68,** 1024; Jour. Cutan. Dis., 1917, **35,** 594.

5. Schamberg, Kolmer, Raiziss and Gavron: Experimental Studies of the Mode of Absorption of Mercury When Applied by Inunction, Jour. Am. Med. Assn., 1918, **70,** 142.

OBJECT OF THE AUTHORS' EXPERIMENTS

Our series of experiments was undertaken to determine, if possible, the extent of absorption of mercury into the circulation as indicated by the elimination in the urine, when the ordinary methods and dosage were employed and the time during which mercury continues to be eliminated in the urine after the mercury has been discontinued. The idea was to determine the frequency and size of the dose necessary to maintain mercury circulating in the body fluids, having assumed, as stated by Meyer and Gottleib, that the excretion of mercury in the urine offers a means of estimating the amount of mercury circulating in the body and that the success of the treatment depends on a certain amount of mercury in the body fluids. The effects of the various forms of mercury on the kidneys as determined by the appearance of protein, casts, or blood in the urine, was also to be estimated when possible.

Our first series of experiments were carried out according to the Elliot[6] method.

This series consisted of the following cases:

REPORT OF CASES

CASE 1.—Baby G., aged 2 weeks, was born with typical syphilitic lesions. A 1:1,000 mercuric chlorid solution was given, 10 drops, three times daily. Mercury was readily detected in the urine after the second day (not examined earlier). The mercury was discontinued and after one week the urine still contained traces. The urine, while this treatment was continued, contained appreciable amounts of protein and granular casts. The symptoms of syphilis rapidly cleared up under this treatment. Two months later, when having mercury ointment under the abdominal band, 0.5 gm. daily, appreciable amounts of mercury were found in the urine. May 17, two weeks after all treatment had been discontinued, distinct traces of mercury were found.

CASE 2.—Baby girl R., aged 5 days, had congenital syphilis. One gram of 33⅓ per cent. mercurial ointment was rubbed into the skin. On the second day mercury was readily detected in the urine and it is probable that it could have been detected earlier if examined.

CASE 3.—Baby boy L., newborn, was given 0.03 gm. of gray powder on December 5. On December 6, 7 and 8 mercury was readily detected in the urine.

CASE 4.—Edna B., aged 25 months, had congenital syphilis. She received 0.03 gm. of gray powder December 5. December 6, mercury was readily detected in the urine, also present December 8.

CASE 5.—Baby boy P., aged 4 days, was given 0.03 gm. of gray powder for three doses on the fourth day. On the sixth and eighth days mercury appeared in the urine.

CASE 6.—Baby girl R., aged 20 months, had congenital syphilis. She received seven inunctions of 0.5 gm. of 33⅓ per cent. mercury ointment before the urine was examined. Urine contained appreciable amounts of mercury.

CASE 7.—Baby boy J., aged 11 months, had congenital syphilis. He received two inunctions of 0.5 gm. of 33⅓ per cent. mercury ointment. Following the second inunction mercury was readily detected in the urine.

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6. Elliot, J. A.: A New and Delicate Method for the Detection of Mercury, Jour. Am. Med. Assn., 1917, **68,** 1693.

RESULTS OF A SERIES OF EXPERIMENTS TO DETERMINE THE ELIMINATION OF MERCURY IN THE URINE

Name and Age	Diagnosis	Form of Mercury	Dose	Date of Treatment	Date of Examination	Amt. of Mercury in Mg.	Remarks
W. A. 21 months	Cerebrospinal syphilis	Gray powder and mercurial ointment	0.03 gm. 1.5 gm. every day for six days	2/22 to 3/8, inclusive	2/28	+	Appreciable amounts of protein in urine
					3/ 1	+	
					3/ 2	+	
				Gray powder discontinued, 3/8	3/ 3	+	
					3/ 7	0.44	
					3/ 8	0.97	
					3/12	+	
				Treatment discontinued, 3/26	3/26	+	
					3/28	+	
					3/29	+	
					4/ 2	+	Elimination of considerable amounts after periods during which there were only traces suggesting stored mercury in some organ
					4/ 8	1.5	
					4/ 9	0.2	
					4/10	+	
					4/12	+	
C. O. 9 years	Endocarditis; edema	Mercurial ointment	1.5 gm. 33⅓% mercury	3/19	3/19	+	
					3/20	+	
					3/21 to 4/5	—	
			1.5 gm. 33⅓% mercury	4/5	4/6	+	Note large amounts of mercury given and little elimination. Did the edema have anything to do with this lack of absorption?
			1.5 gm. 33⅓% mercury	4/6	4/7	+	
			1.5 gm. 33⅓% mercury		4/8	+	Discharged
E. B. 11 years	Congenital syphilis	.....	.....	.....	4/18 and 21	—	Had had mercury long time before
		Mercury salicylate in oil	0.5 c.c. = 0.0325 gm. mercury salicylate	4/25	4/26	0.5	
					4/27	+	
					5/ 1	+	
					5/ 2	+	
					5/ 3	+	
					5/ 4	1.0	Appreciable amounts of protein in urine
					5/ 5	+	
					5/ 6	0.35	
		Mercury salicylate in oil	0.5 c.c. or 0.0325 gm.	5/7	5/ 8	0.5	Shows accumulation in system
					5/ 9	+	
					5/10	+	
					5/12	+	
					5/16	+	
					5/21	+	
B. 5 years	Congenital syphilis	Mercuric chlorid	1:1000 solution, 10 drops three doses only	4/10	4/11	+	
					4/14	+	
					4/26	—	
		Mercury salicylate in oil	0.5 c.c. = 0.0325 gm.	4/26	4/27	+	Appreciable amounts of protein in urine. A few granular and hyaline casts
					4/28	0.4	
					4/29	+	
					4/30	+	
					5/ 1	+	
					5/ 2	0.25	

RESULTS OF A SERIES OF EXPERIMENTS TO DETERMINE THE ELIMINATION OF MERCURY IN THE URINE—(*Continued*)

Name and Age	Diagnosis	Form of Mercury	Dose	Date of Treatment	Date of Examination	Amt. of Mercury in Mg.	Remarks
D. G. 10 years	Chorea minor	Calomel	0.016 gm. four doses	5/10	5/11 5/12 5/13 5/17 5/18 5/19 5/20 5/21 5/22 5/23	+ + + + + + + + + +	Bowels loose. Probably eliminated in feces
L. 9 years	Congenital syphilis; periostitis	Mercury ointment 50	1 gm. on knee and leg daily	Daily up to 4/10, discontinued 4/27	4/11 4/27 4/28	0.54 + —	
		Mercury salicylate in oil hypodermically	0.5 c.c. or 0.0825 gm.		5/ 1 5/ 2 5/ 3 5/ 4	0.25 + + +	
C. N. 15 years	Congenital syphilis; periostitis	Mercurial ointment	1 gm. daily around knee	Daily	4/13 4/27	+ —	All treatment discontinued 4/13
		Mercury salicylate in oil	0.5 c.c. = 0.0825 gm.	4/27	4/28 4/30 5/ 1 5/ 5	+ + + +	Traces of protein in urine. Few casts
C. M. 3 years	Malnutrition	Mercury chlorid	0.5 c.c. of 1% solution hypod.	5/17	5/18 5/19 5/20 5/21 5/22-23	+ + + + +	
F. O. 5 years	Burn; scar	Mercury chlorid	0.5 c.c. of 1% solution hypod.	5/17	5/18 5/19 5/20 5/21 5/22-23	+ + + + —	
J. D. 5 years	Cystitis	Calomel	0.016 gm. for four doses	5/11	5/12 5/13 5/14 5/15 5/16 5/17 5/18 5/19 5/22	0.4 + + + + + + + +	
Boy T. 1 year	Congenital syphilis	Calomel	0.016 gm. for four doses	3/14 3/16 3/17 4/10	3/15	.. + + +	This case had had mercury inunction for considerable time, but it had been discontnued two weeks before calomel treatment
G. C. 8 years	Diabetes mellitus	Mercurial ointment	1.5 gm. 33⅓% mercury	4/4	4/ 5 4/ 6 4/ 9 4/12	1.3 + + +	

RESULTS OF A SERIES OF EXPERIMENTS TO DETERMINE THE ELIMINATION OF MERCURY IN THE URINE—(*Continued*)

Name and Age	Diagnosis	Form of Mercury	Dose	Date of Treatment	Date of Examination	Amt. of Mercury in Mg.	Remarks
J. C. 6 years	Syphilitic periostitis	Mercurial ointment	1.5 gm. 33⅓% mercury	3/12	3/13 3/14 3/15 3/16 3/18 3/19 3/20	1.0 0.10 0.12 0.10 + — —	 Approximately Approximately Approximately
Boy P. 2 days	Normal; newborn	Mercury salicylate in oil	0.5 c.c. = 0.0325 gm.	5/1	5/2 5/3 5/4 5/5	1.0 + 1.0 +	 No further examination
Boy J. 2 days	Congenital syphilis	Mercury salicylate in oil	0.5 c.c. = 0.0325 gm.	5/3	5/ 4 5/ 6 5/10	0.3 + +	 Discharged
Boy M. 5 months	Congenital syphilis	Mercury ointment under band for past month	0.12 gm. mercury ointment	5/1 discontinued	5/ 2 5/ 9 5/16	+ 0.75 +	Treatment discontinued

Several other new-born infants were given mercury by smearing 1 gm. of 33⅓ per cent. mercury ointment on a piece of linen and placing it in contact with the skin under the abdominal band (sealed with wax paper). Owing to the small amounts of urine collected, the results in some cases were unsatisfactory, but in many, positive traces of mercury could be demonstrated. All new-born infants left the hospital on the tenth or twelfth day.

FURTHER EXPERIMENTS

The next series of analyses were made by a modification of Heinzelmann's method.[7] It was necessary on account of the difficulty of securing chemically pure zinc, to substitute aluminum for zinc and dissolve in potassium hydroxid instead of hydrochloric acid. The method is as follows:

To the twenty-four-hour specimen of urine, usually not more than 500 c.c. are used, add 1 gm. of potassium chlorate and 5 c.c. of concentrated hydrochloric acid for every 100 c.c. of urine. Heat over the free flame until the color changes from dark red to light yellow. Cool to 70 C.; add 1 gm. of very fine granulated aluminum and allow to stand over night. Decant and wash twice with about 25 c.c. of water. Dissolve in 5 c.c. of potassium hydroxid, 40 per cent.; when solution is complete add 25 c.c. of concentrated hydrochloric acid. If solution is not complete after some time heat gently, cool, pour into a Hehner cylinder and dilute to 90 c.c. with water; add 10 c.c. of saturated hydrogen sulphid water, mixing with a glass rod, which is bent into a spiral at one end. At the same time prepare a standard, using

7. Heinzelmann: Chem. Ztg., 1911, **35,** 724.

equal amounts of aluminum, potassium hydroxid, and hydrochloric acid adding with a pipet 5 or 10 c.c. of mercuric chlorid solution containing 1 or 2 mg. of mercury. Compare colorimetrically. If the day's specimen of urine is less than 100 c.c., it is diluted to 100 c.c. and carried out as above; if the amount is more than 100 c.c. and less than 500 c.c., it is used without dilution.

SUMMARY AND CONCLUSIONS

From the small series of experiments described in the foregoing charts we have drawn the following conclusions:

In infants and children, mercury, when given by the mouth, by inunction or intramuscularly, is excreted at least partly by the urine.

In new-born infants and older children mercurial ointment when placed in contact with the skin, without any friction being used (protected and sealed by wax paper from being volatilized and inhaled), is taken up by the skin and excreted in the urine and continues to be excreted in the urine for a variable time after all treatment has been discontinued.

By inunction (with rubbing) mercury is readily taken up by the skin and eliminated in the urine and continues to be eliminated for a considerable time.

When one inunction is given, the maximum daily amount of mercury is usually eliminated during the following twenty-four hours, smaller amounts being eliminated for a variable time.

Where continuous inunctions are given there is an accumulation in the system and considerable amounts are eliminated at intervals with only traces between.

It is therefore probable that it is unnecessary to have mercury in contact with the skin, either with or without rubbing as often or as long as has been generally thought necessary. This, however, must be determined by further clinical investigation.

Mercury salicylate suspended in oil and given subcutaneously continues to be eliminated in the urine in appreciable amounts for eight days, or longer, the daily amounts eliminated varying widely. It is therefore probable that a repetition of the treatment, not oftener than at intervals of eight days would be sufficient.

Mercuric chlorid by intramuscular method, a favorite method in congenital syphilis, continues to be eliminated for eight days or longer.

In all cases in which mercuric chlorid was used either by mouth or the intramuscular method protein was found in the urine.

Calomel, 0.016 gm. every two hours for four doses, and gray powder, 0.03 gm. every three hours for 3 doses, continued to be eliminated in appreciable amounts in the urine for as long as nine days; the maximum daily elimination usually occurred during the twenty-four hours following administration. It is therefore probable that

the daily use of any of the mercurial salts in the amounts usually prescribed, is unnecessary and presumably harmful.

We shall continue our investigations and believe it is not too much to expect that in the near future, with the methods now at our disposal of estimating quantitatively the amount of mercury in the body fluids, some degree of accuracy will be attained in the treatment of syphilis by the different mercurial preparations.

We are grateful to Dr. J. P. Sedgwick, who suggested this problem, and for his constant interest in the work.

A CASE WITH VASCULAR, JOINT, MUSCLE AND SKIN DISTURBANCES OF UNCERTAIN ETIOLOGY*

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The subject of this report is a child, aged 4½ years. There are two other children in the family who are normal. The family history is in other respects negative.

CLINICAL HISTORY

This child was perfectly well and had no symptoms until early in November, 1917. At that time she was vaccinated against smallpox. The vaccine used was the same as that employed in many cases without any unusual results. The reaction from the vaccination was violent with high temperature and the involvement of the glands in the groin. A few days after the vaccination had subsided her face became red and swollen about the eyes and she complained of a little stiffness in bending her knees. From that time until early in January there was a steady progress in the condition, until at the present time all the joints of the body are involved including the spine. This condition is shown in Figure 1. Passive motion causes slight pain. It is impossible fully to extend or flex any of the joints. The feet are held in equinus position. The muscles feel as in chronic state of contraction. She does not voluntarily use even her hands. She is able to walk if compelled to do so, but stands on her toes and complains constantly to be put back to bed. The edema and redness about the eyes has persisted (Fig. 2). There have been subconjunctival hemorrhages. The mucous membranes of the mouth about the teeth are red, edematous and hemorrhagic in spots. In appearance they closely resemble the gums in scurvy. Under the arms a macular erythema appeared and progressed to the loss of the superficial layers of the skin in some places and has resulted now in brownish pigmentation (Fig. 3). There is also a larger area of a diffuse pink blush extending down almost to the crests of the ileum and to the anterior and posterior axillary lines. The fingers and toes show at their tips a blotchy erythema resembling Raynaud's disease (Fig. 4). The skin almost everywhere, but more marked on the legs, arms and back, presents a brawny induration. The superficial layers cannot be pulled away

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* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

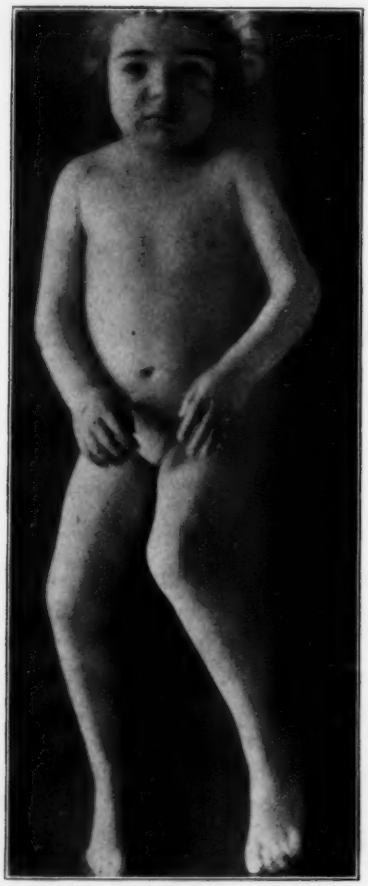

Fig. 1.—Showing the contractures which involved all of the joints of the body, including the spine.

Fig. 2.—Edema with marked redness of the eyes and eyelids.

Fig. 3.

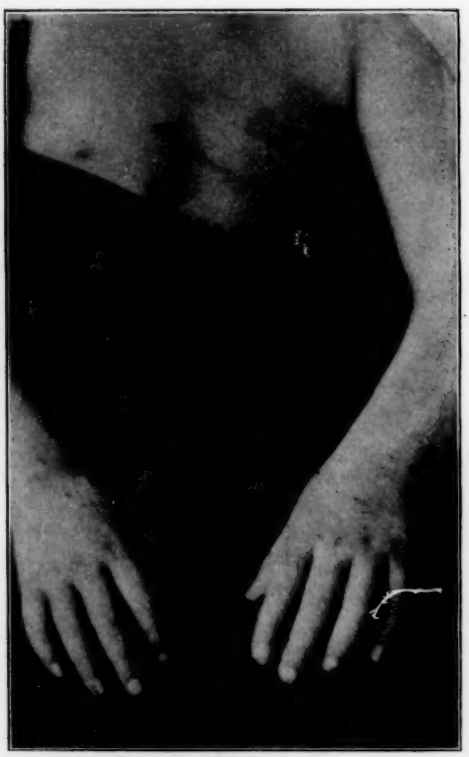

Fig. 4.

Fig. 3.—Pigmented and erythematous lesions in the axilla.

Fig. 4.—Blotchy erythema of the fingers and hands; a condition which resembles Raynaud's disease.

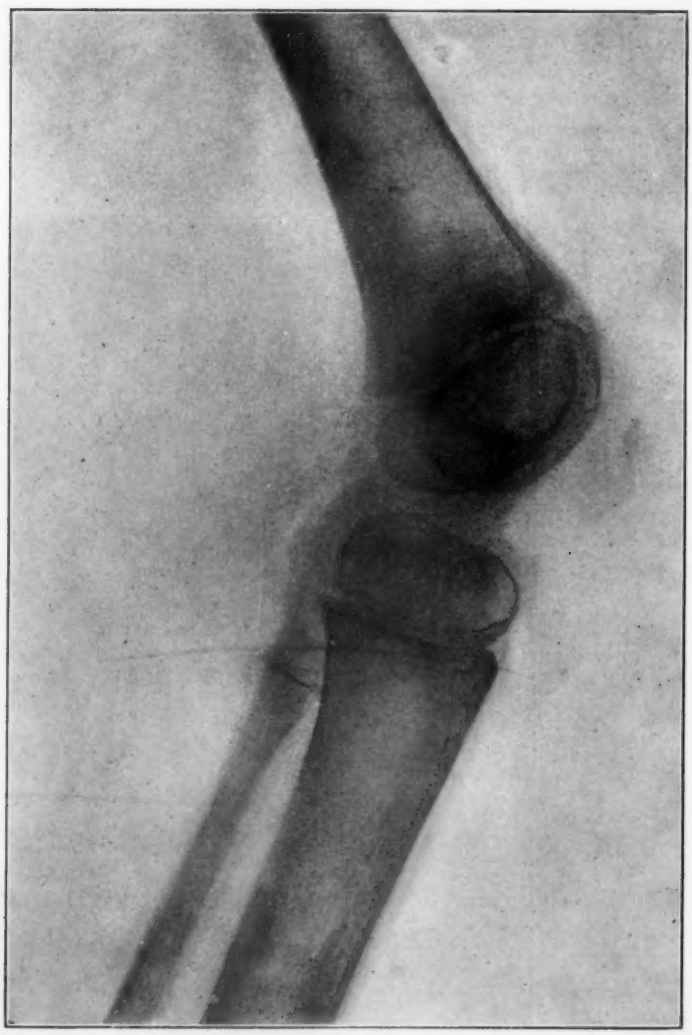

Fig. 5.—Roentgenogram of the knee joint which reveals nothing pathologic, peculiar skin condition seen in plate not visible in print.

from those beneath. In some portions, especially over the sacrum, there is slight edema. The lesions of every kind are absolutely symmetrical even to the position of the erythematous blotches on the finger tips. The skin feels a little dry, but perspiration is present. The hair is rather coarse, but abundant even on the upper portion of the back and on the arms. Previous to the onset of symptoms the child was cheerful and happy, but since the trouble began she has become very tearful, quiet and does not want to be disturbed.

PHYSICAL EXAMINATION

Aside from the lesions mentioned, the physical examination is entirely negative. There has been no fever. The blood is normal. The urine is normal except that in the last two weeks there have appeared a few pus cells and coincident with this a slight rise in temperature. The stool is negative, except at first there was a slight excess of starch. The blood pressure is normal. The pulse rate is 120. The Wassermann test is negative. The Von Pirquet test is negative. The blood culture is negative. The roentgenogram reveals nothing pathologic in the joints (Fig. 5). The selia turcica is normal. The teeth are normal. The subcutaneous tissues show a curious irregular striation unlike anything with which we are familiar.

SUMMARY

The striking features of this case are as follows: The very extensive symmetrical involvement of various portions of the body, the brawny induration of the skin, the vascular disturbance of the skin and mucous membranes, the stiffness of the joints, the roentgen-ray findings in the skin, and the change of disposition.

The etiology of this condition is extremely doubtful. We believe that the vaccination had nothing to do with it. Possibly some toxic agent has affected the glands of internal secretion. No focus of infection has been found. Some change in the vascular system is suggested by many of the findings. The skin may be primary and the other signs secondary to it. The most likely diagnosis seems to us to be a diffuse scleroderma.

So far as treatment is concerned, nothing has been done which has modified the course of the condition in any way. In the last three months there has been very little progression, and in the last few weeks there has been a slight tendency toward improvement.

MIGRAINE IN CHILDHOOD*

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While migraine in later childhood differs in no respect from the disease as seen in the adult, its recognition in infancy and early childhood offers considerable difficulty, owing to the inability of the patient to describe symptoms accurately.

As is well known, migraine is often a hereditary disease, being directly inherited in about 50 per cent. of the cases. Not infrequently it has been known to occur in three or even four generations. It has not yet been ascertained whether or not the mendelian laws govern its inheritance. Like other hereditary diseases, it may be congenital, though this is exceptional. Such was the case with Russell's patient,[1] who had the first manifestations at the age of 2 weeks, with attacks regularly thereafter every two weeks; at the age of 7 years the disease changed to the ophthalmoplegic type.

Age at Onset.—In Flatau's[2] large series of 307 cases, the disease began most frequently from the sixteenth to the thirtieth year, but in 21 per cent. the onset was before this period and in 12 per cent. before the eleventh year. In only 1 per cent. did it begin during the first five years of life. Gowers,[3] however, found a larger incidence in childhood, about one-third of his cases beginning between the fifth and tenth years, and two-fifths between the ages of 10 and 20. All writers agree that it is rare in the first half decade.

Symptomatology.—In infancy the symptoms are obscure and the attacks are of shorter duration than in the adult, lasting only a few hours. There are periodic attacks of vomiting, associated with pain and restlessness, and sometimes convulsions; the temperature is often somewhat raised. Constipation is the rule, in contrast with gastroenteritis, a disease which is in other respects somewhat similar to migraine at this period of life.

In early childhood the attacks are more like those in the adult, though the pain is less often localized in one side of the head, and sensory and ophthalmic symptoms are less common. Of great interest is the association with cyclic vomiting, which is apparently not very

* Submitted for publication Aug. 26, 1918.
* Read at the meeting of the American Pediatric Society, Lenox, Mass., May 28, 1918.

1. Russell, J. W.: Brit. Med. Jour., 1903, **1**, 1020.
2. Flatau, E.: Die Migräne, Berlin, 1912.
3. Gowers, W. R.: Diseases of the Nervous System, Ed. 2, 1898, **2**, 836.

uncommon. Usually cyclic vomiting appears first and is replaced later in childhood by migraine, but in the case of Comby[4] migraine appeared at the age of 2, and was replaced by cyclic vomiting at the age of 8, while in one of Fabre's[5] cases, a girl of 9, migraine came first, but did not cease with the appearance of cyclic vomiting.

The association with epilepsy is rare in childhood.

Increased intestinal putrefaction is a rather frequent accompaniment of migraine which is often overlooked. While it is not constant, and therefore cannot be the cause of the disease, it appears to aggravate the attacks, and hence is worthy of consideration. The examination of the urine for phenol will often reveal such putrefaction where the test for indican is negative. It cannot be too strongly emphasized that the amounts of phenol and of indican in the urine are quite independent of one another. The reason for this is that phenol is derived from the tyrosin portion of the protein molecule, while indican is derived from tryptophan. It is possible that one set of intestinal micro-organisms attacks tyrosin, and another tryptophan. A simple test for phenol in the urine is the following: 100 c.c. of urine are distilled with 5 c.c. of strong sulphuric acid until one-half of the liquid has gone over, and to the distillate is added bromin water in excess. The presence of a definite white precipitate (tribromphenol) indicates the presence of phenol in excessive amounts.

Recent work by Folin and Denis[6] and by Dubin[7] has thrown new light on the physiology of the phenols. This has been rendered possible by a new colorimetric method, devised by Folin and Denis,[8] by which phenol, both free and combined, can be determined rapidly, and with accuracy. Contrary to the long-prevailing opinion, Folin and Denis have shown that the greater part (about 80 per cent.) of the phenol in the urine is normally excreted in the free state. Dubin, however, found that if phenol is administered in large amounts to dogs, a very marked increase in the conjugation takes place. It would appear, therefore, that the protective mechanism by which phenol is rendered harmless is called into play only when excessive amounts have to be cared for. The total amount of phenol, both in animals and in man, was found to vary directly but not proportionally with the intake of protein. After the use of enemas and of cathartics the amount is lowered appreciably.

The nature of migraine is still little understood. The analogy with epilepsy is very close; in both conditions there is a strong heredi-

4. Comby, J.: Arch. de méd. d. enf., 1901, **4,** 9, Observation 11.
5. Fabre, E.: Migraine chez les enfants. Thèse de Paris, 1904.
6. Folin, O., and Denis, W.: Jour. Biol. Chem., 1916, **26,** 507.
7. Dubin, H.: Jour. Biol. Chem., 1916, **26,** 69.
8. Folin, O., and Denis, W.: Jour. Biol. Chem., 1915, **22,** 309.

tary element; in both periodic cerebral attacks, affecting in the one case the sensory, in the other the motor sphere. Moreover, the two diseases often have been found in the same person, migraine occurring first, being replaced later by epilepsy.

A comparison with asthma, another hereditary disease, suggests another point of view. Here again are periodic attacks, with intervals of good health. The symptoms of asthma resemble closely those of anaphylactic shock in the guinea-pig, and for many cases a hypersusceptibility to certain proteins has been demonstrated. It has been attempted to explain migraine also as a manifestation of anaphylaxis, but thus far without success. It is true that indiscretions in diet may precipitate an attack of migraine, and that a low protein diet is beneficial in some, though by no means in all cases, but hypersusceptibility to proteins has not been shown by direct methods, eosinophilia has not been reported, and the symptoms are not similar to those of experimental anaphylaxis.

A disorder of metabolism is another possibility, for which there are analogies among inherited diseases, such as diabetes and gout, in which there is direct heredity, and those rare anomalies of metabolism, pentosuria, cystinuria and alkaptonuria, in which, however, the condition is congenital and familial but not hereditary. Moreover, diseases of metabolism may show marked periodicity, as in gout, and that rare disease known as family periodic paralysis, in which Edsall and Means[9] have recently shown decided disturbances of metabolism, in the shape of increased basal metabolism during attacks, and a long continued marked increase of the nonprotein nitrogen of the blood, in the absence of nephritis. Very little work has been done on the metabolism in migraine, and this should offer a good field for future investigation.

It often has been attempted to explain the symptoms of migraine on the basis of an abnormal reaction of a diseased central nervous system to stimuli which in the healthy person would produce no effect. In favor of this view various signs of a disturbed vasomotor and sympathetic innervation during the attack have been adduced. But this theory altogether fails to explain the most striking feature of migraine, namely, the periodicity of the attacks, and the sense of well being during the intervals.

To sum up, the cause of migraine remains obscure. The hypothesis of intoxication by the products of a disordered metabolism seems at present to offer the best basis for investigation.

Diagnosis.—The diagnosis rests chiefly on the periodic occurrence of headache, accompanied usually by nausea and vomiting. The

9. Edsall, D. L., and Means, J. H.: Am. Jour. Med. Sc., 1915, **150,** 169.

intervals between attacks vary from one to two weeks up to several months in duration, and are free from symptoms, unless the attacks follow one another very closely. It is not essential that the headache should be confined to one side; in case it is not, it is usually frontal, rarely occipital. Scintillating scotomas, numbness of one side of the body and other ophthalmic and sensory symptoms are not a necessary part of the disease, and in fact are rare in childhood. A family history of migraine is of much diagnostic value. In young children the diagnosis may be difficult on account of their inability to describe symptoms. The periodicity of the attacks, however, and the state of well-being between them, together with the exclusion by careful physical examination, of other causes of headache, will usually enable one to arrive at the correct conclusion.

From cyclic vomiting it is differentiated by the following features: in migraine the headache precedes the vomiting, and is the predominating symptom, while in cyclic vomiting the headache is usually not severe, and the vomiting is frequent and intractable. The presence of large amounts of acetone in the urine is constant in cyclic vomiting, and also in migraine providing vomiting is present, but in the former it may precede the attack, and in that case has diagnostic value.

Treatment.—A thorough examination of the patient, with especial attention to the eyes, nose, throat, accessory sinuses, teeth and digestive tract, is a prerequisite of intelligent treatment. While it is doubtful if true migraine has ever been cured by the correction of refractive errors, of nasal troubles or by alterations of the diet, it is true that any measure that improves the patient's general condition is likely to ameliorate the severity of the attacks, and to reduce their frequency. For this reason any abnormalities which are capable of correction should receive attention.

The diet is of considerable importance. It is well known that some persons have fewer attacks if meat and fish are excluded. This effect was formerly attributed to the influence of a purin-poor diet on the uric acid diathesis, which was erroneously supposed to play an important part in migraine. It may well be due to the reduction of an increased intestinal putrefaction, a factor which should always be looked for. If it is present, meat, fish and eggs should be excluded from the diet, and the effect on the excretion of phenol and indican noted. In some cases it may be even necessary to exclude milk to attain the desired result. Constipation, if present, of course should be corrected, as tending to increase intestinal putrefaction.

In a few cases attacks apparently are precipitated by overindulgence in corbohydrates, such as candy.

Attention to hygiene is an essential part of the treatment. It is often necessary to withdraw the child from school for a while, and to limit

the hours of study and reading. An abundance of fresh air and exercise in amounts suited to the individual are indicated.

The use of drugs during the attack should be limited, since in small doses they have no effect, and in large doses they are apt to be deleterious. Of the antineuralgics, caffein seems to have the best effect. Morphin may be required in very severe paroxysms. The administration of drugs during the intervals, with the purpose of reducing the severity and frequency of attacks, has proved disappointing in my hands, though recommended by Oppenheim and other authorities.

By the use of the above measures the frequency and severity of the attacks are usually lessened, but it is doubtful if true migraine is ever cured.

The following case seems worthy of report on account of the unusually early incidence of the disease and the presence of large amounts of phenol in the urine.

REPORT OF CASE

History.—H. B., a boy, aged 6 years, was seen March 1, 1918, in consultation with Dr. H. M. Steele.

Family History.—The maternal grandmother and a maternal aunt have suffered severely from typical migraine. The parents and a sister aged 4 years are free from headache.

Past History.—This is negative except for the fact that as an infant he used to lick the paint off the bed.

Present Illness.—Since the age of 3 years, he has been subject to periodic attacks of headache, accompanied by vomiting. Acetone occurs abundantly in the urine at these times, a feature which had led to the diagnosis of cyclic vomiting. The attacks come at intervals of from one to three months, as a rule, but during the previous winter have occurred about once a week. There is an aura the day before, consisting of pallor, nervousness and an abnormal appetite, usually poor, but sometimes increased to a pathologic degree. The headache is intense and always precedes the vomiting; it is bilateral and frontal in distribution and accompanied by photophobia. The duration of the attack is about twenty-four hours. Between attacks the boy is well and free from headache. There has been a distinct intolerance of eggs; if he takes more than one egg a week he is almost certain to have an attack. He has not taken large quantities of meat.

Physical Examination.—A fairly developed boy, 45 inches in height, weighing only 37 pounds (the normal weight for this age is 45 pounds). The head is rather square, but there are no other signs of rickets. The tonsils are moderately enlarged. The heart, lungs, abdomen and reflexes are negative. The systolic blood pressure measures 82 mm., the diastolic 50. The examination of the eyes by Dr. E. M. Blake, shows a considerable degree of hypermetropia (+2 D.). The hemoglobin is 90 per cent. The blood smear shows a considerable increase in lymphocytes, the count being as follows: polynuclear nuclears, 35 per cent.; lymphocytes, 58.5 per cent.; large mononuclear and transitional cells, 4 per cent.; eosinophils, 1 per cent., and mast cells, 1.5 per cent. The red cells are normal.

Urine: Twenty-four hour amount, 500 c.c., color normal, reaction acid, specific gravity 1.015, albumin sugar and indican absent, *phenol present in large amounts,* acetone present (during the attack), sediment negative. Examination of the feces for lead is negative.

Treatment.—The treatment consisted in withdrawal from school, the correction of the refractive error and alteration of the diet. Throughout the month of March no meat or fish was eaten. During April the child was put back on his former diet. It was now found that he had an increased tolerance for eggs, which he craves, being able to take three or four a week without headache. Examination of the urine April 16 and May 22 still showed large amounts of phenol; during March, when the protein intake was restricted, no examination was made. In spite of the phenoluria he has been practically free from headache since beginning of treatment, having had but one slight attack from March to the date of writing, June, 1918.

COMMENT

The beneficial effect of even a temporary diminution of the protein intake is shown in the almost complete disappearance of the headaches, and in the increased tolerance of eggs. Further restriction of protein is indicated, until the excretion of phenol reaches normal limits.

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PROGRESS IN PEDIATRICS

RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF CHILDHOOD*

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In surveying the literature of the past year in these fields one's attention is caught by the notably large number of contributions that deal with problems of nutrition in childhood, by the number of articles on hypertrophic stenosis of the pylorus in infancy, and by the unusually large number of fetal anomalies that are reported.

That there should be numerous articles dealing with problems of nutrition is but natural and is a reflection of the importance of the subject in a time of changing and often restricted dietaries. Careful study of all the conditions surrounding infancy and childhood, birth, nutrition and growth, is stimulated by the insistent call for men that comes from all the warring nations. It is clear that if there are to be healthy, efficient men in the future, there must be well-born, well-nourished infants, in the present.

PHYSIOLOGY

Birth Rate.—In his address as a retiring sectional vice president of the American Association for the Advancement of Science, Louis I. Dublin,[1] statistician of the Metropolitan Life Insurance Company, discusses in an able manner the significance of the declining birth rate. The condition is not peculiar to any one nation. It affects not only the gross totals of population, but also the internal structure of population. In the presence of a declining birth rate, youth and strength come to form a smaller part of the total population, the old and dependent form a much larger part. Moreover, the reduction of birth rate is found to have affected mostly those who are both economically and socially best fitted to bear and to raise a family.

In order that a national stock may maintain itself without increase or decrease it is found that the average number of children in the family must be close to four. At first thought it might seem that something over two children per family would suffice to maintain the stock. That this is not true is due to three facts: (1) not all persons

* Submitted for publication Sept. 26, 1918.

1. Tr. Am. Assn. for Advancement of Science, 1918.

marry; in America, 12 to 15 per cent do not marry until after the reproductive period, if at all; (2) a considerable proportion of marriages, over 7 per cent., are sterile; (3) the death rate is exceptionally high in the period of childhood, amounting in the first year of life to about 10 per cent. of the babies born, and continuing, at diminished rates, until at the average age of marriage there are only 73,000 individuals left out of every 100,000 born.

From a national point of view the situation in America is made worse by the fact that it is the native stock that is declining. A tabulation based on the population returns of the 1910 Census shows that while in a group of women under 45 years of age who were married for a period of ten to twenty years the average number of children was 4.1 per married woman, the woman of native parentage showed an average of only 2.7 children per married woman. Moreover, the women of native parentage had borne no children in 13 per cent. of the cases, the women of foreign parentage in only 5.7 per cent. of the cases.

Among our college bred women the number of children per married woman is strikingly small—Smith College, 1.3; Vassar, 1.6; Bryn Mawr, 1.7; Holyoke, 1.8; figures that are all the more significant since less than 50 per cent. of the graduates of women's colleges marry. Studies of the families of 643 American men of science by Cathell, show that these men came from families that had an average of 4.7 children; their own families, where the men were married and their families were complete, showed an average of only 2.3 children, these figures including all the children born.

It is clear that this decrease in our national stock is due to the exercise of conscious limitation of births. Our national stock is being replaced by a stock of a different order. Our national standards, says Dr. Dublin, are being leveled to meet more and more the lower quality of our population.

The matter is one that vitally concerns the individual and the society of individuals, the state. It is suggested that the state may lessen the evil by providing a more rational education, by inculcating national ideals, by making our various national groups conscious of their best traditions and instilling desires to see their better strains strengthened and increased as a foundation of the greater democracy of the future.

The economic and social burden that is now laid on the man and woman who bears the requisite number of children must be lessened. The mother of several children should be favored with the admiration of the community in which she lives, not with its commiseration and pity. It may be found expedient for the state to encourage parenthood

by considering the size of the family, as a factor, among others, in fixing exemptions from taxes. The need of conscious and deliberate birth release among the healthy and normal people of the country is emphasized as primary national duty.

Hamill[2] points out that in every warring country the number of children will continue to decrease in proportion to the number of men called to arms, the number of women taken into industry, and the increase of price in the essentials of life. The various nations face (1) a decreasing birth rate; (2) increasing death rate, and (3) an appalling destruction of adult life in the field of battle. Thousands of men will be totally incapacitated, many more thousands will be only partially capable in years to come. Death and wounds from battle can not be materially lessened so long as the war continues; an increase in the birth rate in war time is not possible; the one possible solution lies in so reducing the infant death rate as to, at least in part, compensate for the loss of population that the other conditions are producing. The attention of nations is thus focused on the available means of saving infant lives. By rendering her governmental agencies more efficient, by increasing her health visitors to one to every five infants born, by granting votes of money to private welfare agencies, so that instead of curtailing they might extend their work, England reduced her infant death rate for 1916, to 91 per thousand living births, a saving over the former year of over nineteen lives in every thousand born. England then was able in 1916 to compensate in a large part for her decreasing birth rate. Hamill estimates that in Pennsylvania alone it would be possible to save about 6,000 babies' lives yearly. A definite health campaign that will carry the necessary information directly to the mothers seems to be the most effective means of combating infant mortality.

Beitler[3] cites Karl Pearson's estimate that for every 1,000 liveborn children, there are 605 stillborn. Mall believed (personal interview) that the incidence of stillbirths is at least one-half of the total number of live births. He says that "out of 58,089 deaths under one month in the registration area in 1910, 25,672, or 61.40 per cent., were attributed to antenatal causes." It is axiomatic that the cause of the mortality from the first to the eleventh day of life is determined almost entirely by prenatal causes.

Birth, Weight and Growth.—Warren[4] reports that in 2,000 con-

2. Hamill, S. McC.: Influence of War on Infant Mortality and Its Meaning, Am. Jour. Med. Sc., 1918, **155,** 1.

3. Beitler, F. V.: Reduction of Infant Mortality Due to Prenatal and Obstetric Conditions, Am. Jour. Obst., 1918, **77,** 481.

4. Warren, S. P.: Average Birth Weight in 2,000 Confinements. Am. Jour. Obst. and Dis. Women and Child., 1917, **76,** 932

finements occurring chiefly in his private practice (State of Maine, 1874 to present time) the average birth weight has been 8¼ pounds for girls, and 8¾ pounds for boys. The mothers belonged to every grade of life, both rich and poor. The average weight of children of foreign born mothers exceeded that of native born American mothers by four-tenths of a pound. It is Warren's experience that babies weighing 10 or 12 pounds at birth are quite frequent in Maine, a condition possibly explained in part by the fact that the state abounds in men and women of large stature, though this would not apply to the foreign element. Balantyne (Antenatal Pathology) says: "The factors of fetal nutrition are so numerous and their relations are so intricate, that it is impossible to arrive at the coefficient of nutrition, so to speak."

Hammett[5] studied the relation between weight at birth and early growth as shown in 537 infants. The data were collected from the records of the Boston Lying-In Hospital, and showed the weight of the infants on the first, third, fifth, seventh, ninth, eleventh and thirteenth days after birth, excluding from consideration those whose food supply was derived either wholly or in part from sources other than the maternal breasts. The infants studied were divided into groups: one hundred infants weighing 5 to 6 pounds, one hundred 6 to 7 pounds, etc. The results recorded in the paper are based on the weights at birth.

The postnatal per cent. loss was found to vary directly with the weight at birth. With the exception of the heavier infants, the third day after birth marked the beginning of the pick-up to the normal rate of growth characteristic for the individual groups. After the third day the per cent. additions to the initial birth weight made between successive weighings shows a steady increase, and one that is greater in the case of the smaller infants.

Hammett[6] points out that Osborne and Mendel, McCollum, and others have shown that the nature of the food ingested is one of the very important factors concerned in growth, that no experimental evidence has yet been presented in support of a theory that the milk elaborated by a mother is not that biologically adapted to the needs of the young of the same species, and that any attempt to determine the fundamental biologic laws of growth during early infancy should recognize this. The factors influencing milk production are manifold. The nutritive condition of the mother, the maternal metabolism, health or disease, all contribute their quota. Nevertheless, during the first two weeks of lactation the variations in the chemical composition of human milk have a remarkably uniform tendency, "and where changes

5. Hammett, F. S.: Relation Between Weight at Birth and Growth Capacity. Am. Jour. Physiol., 1918, **45,** 396.

6. Hammett, F. S.: Jour. Biol. Chem., 1917, **29,** 381.

in the weight of the infant do not indicate supplementary feeding necessary, it can reasonably be assumed that the nourishment is sufficient and characteristic."

As the result of his study the author offers the following conclusions:

> The growth capacity of human infants during the first two weeks after birth is in a large degree dependent on the weight at birth. It is roughly inversely proportional to the initial weight. The ability to recover and pass the initial weight after the postnatal decline obviously varies in the same way, so that at the completion of the period studied (first thirteen days after birth) some 82 per cent. of those infants weighing between 5 and 6 pounds at birth have recovered or passed their initial weight, as compared with 20 per cent. of those weighing from 10 to 11 pounds. The intermediate groups vary inversely as to their weight at birth.

The result of a study by Camerer[7] seems to indicate that differences in growth are similarly correlated with differences in inital weight throughout a much longer period, for he found that in a series of 138 cases, divided into three groups, according as they weighed under 2,000 gm. between 2,000 and 2,750, and over 2,750, and studied after weekly weighings, that the percentage increment of the subjects in the first group was 427, of the second 219, and of the third and heaviest only 195.

It may be noted in passing that 65 per cent. of the infants in Hammett's series weighed between 6 and 8 pounds at birth—30.3 per cent. between 6 and 7 pounds—34.7 per cent. between 7 and 8 pounds. Numerous references to the theoretical aspect of the subject are embodied in this paper.

Bleyer[8] quotes from recent authors to the effect that while we now possess a fairly accurate and extensive knowledge of the normal curve of growth of certain animals, particularly the white rat and white mouse, we are not yet in possession of equally reliable and extensive data concerning the growth of human beings. The most important contribution on periodic acceleration and retardation of growth in children is doubtless that of Malling-Hansen.[9] This study was preceded by the work of Fleischmann, Vierordt, and, particularly, Camerer, and followed by that of Vahl, Buffon, and Godin. Malling-Hansen was able to divide the year into three periods which seemed to him quite well defined. A period of minimal growth was found to occur between mid-April and mid-July, a period of maximal growth between mid-July and mid-December, and a period of mean growth, the so-called "rest period," from mid-December to mid-April. The

7. Camerer: Jahrb. f. Kinderh., 1901, **53,** 281.

8. Bleyer, A.: Periodic Variation in Rate of Growth of Infants. Arch. Pediat., 1917, **34,** 366.

9. Ueber periodic Gewicht des Kindes. Copenhagen, 1883.

differences between these were found to be very great, growth in the maximal period being twice or even three times as great as that in the minimal period.

Bleyer made a simple tabulation of the weights of 1,000 babies who attended a conference for well babies in St. Louis. Records were selected of infants showing normal temperature on the day of weighing, and an absence of recorded illness, both on the day of weighing and the next preceding visit to the conference. Because of the need of dealing with the well babies, no records were used which showed a loss of weight. Half the infants were in the first year of life, and half in the second. Altogether 3,800 weighings were tabulated; they were fairly evenly distributed through the various months of the year and were collected through a period of five years.

The gains were averaged on a basis of grams per day and then transferred for greater convenience into grams per week. Charts were prepared showing the average weekly gains, month by month, of infants in their first, and infants in the second year. A definite seasonal variation is seen. In the second year where the variations were much more marked a definite coincidence with the findings of Malling-Hansen is seen. In the first year the variations were not very great, though sufficient to show the rule. It was found that they were less marked in breast fed infants than in those that were artificially fed.

Following the division into periods suggested by Malling-Hansen, it was found that in the second year the average weekly gains from April to July were 77 gm.; from August to November, 113 gm.; from December to March, 86 gm. These and the preceding figures are presented in tabular form.

No scientfic support was found for any of the various hypotheses that have been advanced to explain the phenomenon of periodic variation in the rate of growth. The view that the acceleration is due to change of diet would not seem to apply to infants, because in the first year no change is usually made, nor is the diet largely different in the summer in the second. It is noted that St. Yves Ménard and also Cornevin observed acceleration in the rate of growth in cattle in summer and fall, and found that this occurred independently of a change in diet.

The following conclusions are offered:

First, periodic variation in the rate of growth, consisting of an acceleration from midsummer to late fall, a retardation in winter and greater retardation in spring and early summer, was found to exist among infants.

Second, this would not appear to be due to change of diet.

Third, weight gains in the first year of life were greater in summer and fall than in winter and spring, and in the second year of life the best gains were

made in August, from which it would not appear that heat has a retarding effect on the rate of growth, but may even favor it.

Fourth, it would seem that the external factors of growth may have to be taken into account in constructing normal weight curves for the first and second years of life.

Anthropometric photographic control of children's growth is discussed by Jeanneret and Messerli.[10]

Metabolism of the New-Born.—Talbot[11] points out that while there has been an increasing amount of investigation of the metabolism of the new-born infant during the past few years, only recently has enough evidence been accumulated to be of any practical value to the general practitioner. Discussion of the subject requires clear understanding of some technical terms, such as "basal metabolism," "respiratory quotient," "energy requirements," etc.

Basal metabolism, as defined by Talbot, means the energy production of an infant in complete muscular repose. It may be obtained only when the baby is asleep. Ideally it should be determined when the stomach is empty, but this is rarely possible in infants, as they usually sleep only when the stomach is full.

The *respiratory quotient* means the volume of carbon dioxid expired, divided by the volume of oxygen used. It has been found that when pure carbohydrate is burned up outside the body the volume of oxygen necessary for its combustion is always the same as the volume of carbon dioxid given off as the result of the combustion; the respiratory quotient of carbohydrate is therefore 1.00. The respiratory quotient of fat is 0.713 and of protein 0.801. Tables have been made from which the amount of the different food components that are being burned up in the body may be estimated, for each respiratory quotient. For example, when a respiratory quotient is 0.90, two-thirds of the energy used up comes from carbohydrate and one-third from fat.

The *energy requirements* of an infant, for example, is the amount of available energy expressed in terms of calories per kilogram required by the body to maintain the vital activity and keep the body warm. The *basal energy requirement* is the amount of energy, again expressed in calories, required to meet the needs of an infant in a state of complete muscular repose; that is, to meet the needs of basal metabolism.

Talbot finds that the *basal* energy requirement of infants from one-half to 6 days of age is 44 calories per kilogram of body weight, whereas the average of a 4 to 5 months old infant is in the neighborhood of 55 calories. The actual requirement for a new-born baby is approximately 62 calories per kilogram of body weight. The

10. Jeanneret, L., and Messerli, G.: Anthropometric Photographic Control of Children's Growth. Rev. méd. de la Suisse romande, 1917, **37,** 570.

11. Talbot, F. B.: Physiology of New-Born Infant. Am. Jour. Dis. Child., 1917, **13,** 495.

requirements rise as he grows older, continuing to do so until about the third month, and then diminishing. Energy production in the form of body heat is a large factor in determining the requirements. The amount of heat produced depends on the amount of *muscle* and the "active protoplasmic tissue" in the body. The presence of a large amount of fat, an inert tissue, so to speak, diminishes the heat production per unit of body weight. The low requirement of the new-born infant is probably related to the disproportionately large amount of fat present in the body of the normal infant; as he grows muscles begin to replace the fat and come to represent a larger proportion of the body weight.

The basal metabolism may also be calculated per square meter of body surface (determined, for example, by Lissauer's formula), or as total heat per twenty-four hours. Talbot finds that shorter infants produce less heat per square meter of body surface, than do longer infants, after the first day and a half of life. He divided the heat production per square meter of body by the length of the infant, and the average of the resultant figure was 12.65 calories. Taking the figures as a constant he offers the following formula for determining the energy requirements:

Total calories = length $\times$ 12.65 $\times$ body surface.

The earliest study of the respiratory metabolism of the new-born infant— it is from the respiratory metabolism that Talbot calculates the energy metabolism—was made in 1877 by Forster.[12] The most important subsequent investigations were published in Danish (Hasselbach, 1904) in such inaccessible form that they were overlooked. They have recently been translated into English and published by the Carnegie Institute of Washington.

The new-born infant does not receive food enough to supply the necessary energy to keep it warm. The body utilizes the glycogen stores of the liver and tissues. This is soon exhausted and the energy is then obtained from the body fat. The destruction of the body tissue contributes to the so-called physiologic loss of weight, part of which is mechanical and part truly physiologic. Anything that protects the infant from unnecessary loss of heat on the one hand, or that supplies a satisfactory source of energy on the other hand, should diminish this loss. Talbot suggests the omission of the routine bath, substituting a cleansing of the body with warm oil, and advocates the feeding of weak or premature infants with breast milk, or, when this is lacking, with temporary feeding of a 5 per cent. solution of some sugar such as lactose.

12. Forster: Amtlicher Bericht der 50 Versammlung deutsche Naturforscher u. Aerzter in München., Munich, 1877, p. 355.

Murlin[13] criticises this in saying that fat does not replace active tissue, but replaces water. "Hence we are driven back on the old explanation which Rubner himself gave, namely, that the lean infant has the higher metabolism because he loses heat faster. He has a larger surface in proportion to weight, and, since it is through surface that heat is lost, it will be in proportion to surface that heat must be produced if the body temperature is to remain constant."

Nutrition in Children.—In a recent article on "The Fundamental Requirements of Energy for Proper Nutrition," Graham Lusk[14] points out that our knowledge of different portions of the subject varies greatly in accuracy. Certain portions of our data "are matters of established fact, repeatedly confirmed; others are based on unconfirmed observations of individual authorities, but probably correct; while still others are based on estimates as close to the actual state of affairs as one can now attain." Our data on basal metabolism of all ages and sexes may be regarded as absolutely accurate, as also, the increase in metabolism due to (*a*) standing; (*b*) walking; (*c*) carrying a load (in adults). On the other hand, our data on the metabolism of children during exercise is to be classified as hypothetic.

Graham Lusk presents a table (Table 1) showing the metabolism of boys from birth to 16 years of age. The curves are based on data for the child at birth (Bailey and Murlin, Benedict and Talbot[15]); data showing a basal metabolism of 48 calories per kilogram of body weight for boys of from 6 to 12 months (Murlin and Hoobler[16]); 60 calories per kilogram for boys of 2 years (Magnus-Levy and Falk's[17] report on the metabolism of a boy 2½ years weighing 11.5 kg.); boys of from 6 to 16 years as shown in curves by Du Bois[18] and in the data showing that boys of 12 years have a basal metabolism of 50 calories per square meter per hour, and at 14 years of 44 calories for the same unit of measure. The metabolism of girls has never been investigated.

As presented in the table the amount of food expressed in terms of total available calories that must be supplied to meet the demands of basal metabolism (see foregoing definition) rises rapidly until the end of the second year, when it reaches 800 calories for a child weighing

13. Murlin, J. R.: Metabolism of Mother and Offspring Before and After Parturition. Am. Jour. Obst., 1917, **75,** 913.

14. Lusk, G.: Jour. Am. Med. Assn., 1918, **70,** 821.

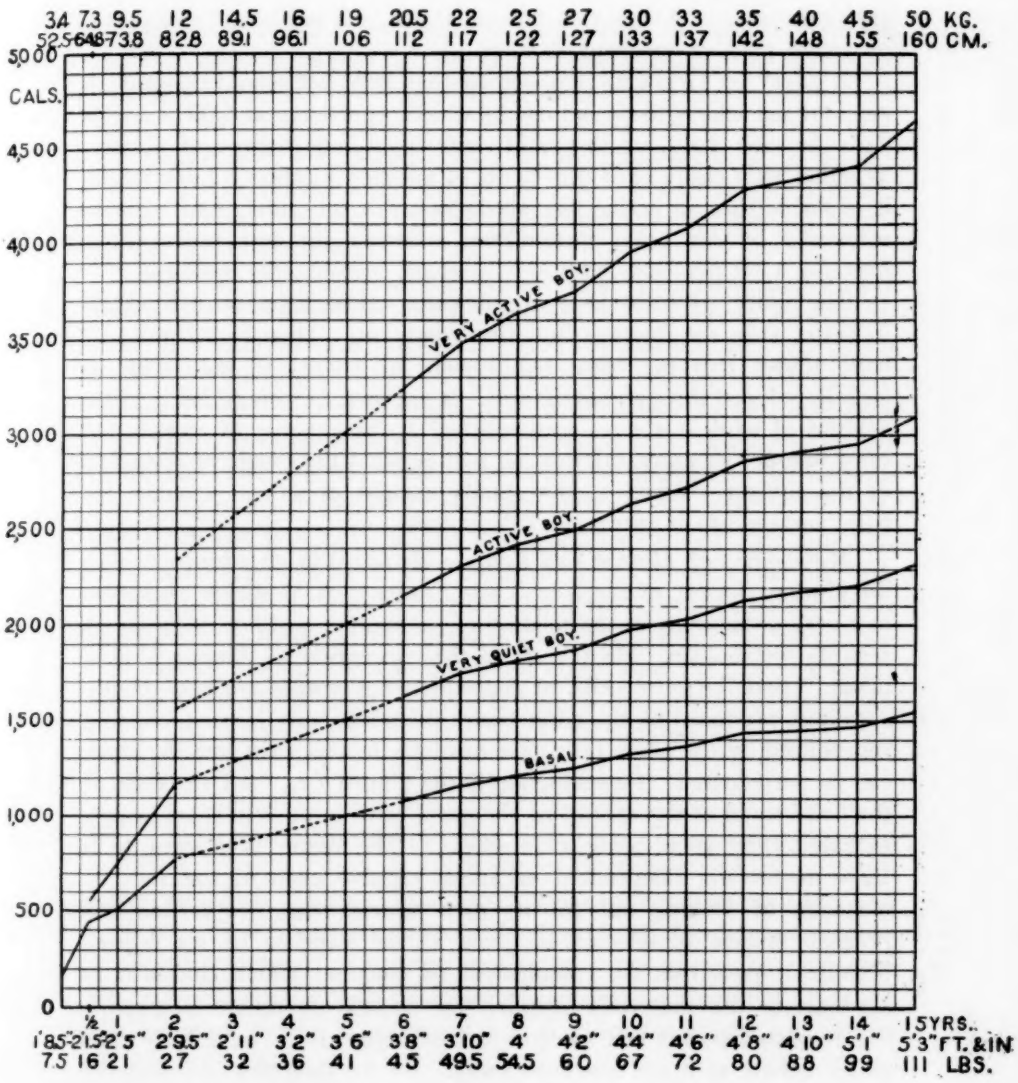
15. Bailey and Murlin: Am. Jour. Obst., 1915, **71,** 526. Benedict and Talbot: The Physiology of the New-Born Infant. Carnegie Institution of Washington, 1915, Pub. 233.

16. Murlin, J. R., and Hoobler, B. R.: The Energy Metabolism of Ten Hospital Children Between the Ages of Two Months and One Year. Am. Jour. Dis. Child., February, 1915, p. 81.

17. Magnus-Levy and Falk: Arch. f. Physiol., 1899-1900, Supplement, p. 368.

18. Du Bois, E. F.: The Metabolism of Boys 12 and 13 Years Old Compared with the Metabolism at Other Ages. Arch. Int. Med., June, 1916, p. 887.

TABLE 1.—METABOLISM IN CALORIES PER DAY OF BOYS FROM BIRTH TO 15 YEARS OF AGE



12 kg., or 26½ pounds; and thereafter rises gradually until at 15 years of age 1,500 calories is needed for a boy of 110 pounds weight.

To this basal requirement must be added something for growth—15 per cent. of the total calories in infancy; and an additional increment for work, etc., whether this takes the form of crying (severe crying increases the basal metabolism 40 per cent. per hour in infancy), or active play, or mechanical labor.

A study by Gephart[19] has shown that boys between 13½ and 16 years of age who actively indulge in athletic sports ingest 5,000 calories daily in their food, or threefold their basal requirement of energy. Whether they really need this or not is another question. Lusk thinks it probable that an active boy produces twice the number of calories measured by his basal metabolism, whereas for one taking little exercise a 50 per cent. additional amount undoubtedly suffices.

The figures given by Lusk are maximal values based on individuals in better than the average nutritive condition. Allen and Du Bois[20] have shown that the basal requirement of energy in men may be largely reduced through emaciation. It appears, however, that a given amount of work is always accomplished at the expense of exactly the same amount of extra calories, no matter what the nutritive condition of the subject. When a man stands upright or sits in a chair, his basal metabolism is increased 10 per cent.

Metabolism of Mother and Fetus.—Murlin,[21] in an address before the Harvey Society of the New York Academy of Medicine, considers in a very broad manner the relation of the mother and her offspring as regards metabolism. He reverts to the conception of August Weissmann:[22] that the germ cells, or reproductive elements are not, strictly speaking, produced by the adult body; the adult body is produced and reproduced by the germ cells as a medium in which the specific stock can be perpetuated. Reproduction is the aim of life. All the cells of the body stand at the service of the germ cells because in them is perpetuated their own being (Hatschek). The ovum is always to a large degree an independent organism capable even in the face of obstacles of looking out for its own nourishment. A certain cell in each follicle is selected to grow at the expense of its fellows because it possesses the complement of enzymes which enable it to appropriate the materials supplied by its less fortunate neighbors. On fertilization this cell receives a fresh impetus. The follicle cells which adhere to it are dissolved away. By the time this is completed

19. Gephart, F. C.: Report of a Dietary Study of St. Paul's School. Boston Med. and Surg. Jour., 1917, **176**, 17.

20. Allen, F. M., and Du Bois, E. F.: Metabolism and Treatment in Diabetes. Arch. Int. Med., June, 1916, p. 1010.

21. See footnote 13.

22. Weissmann, A.: The Germ Plasm, English Translation, London, 1893.

the fertilized ovum has normally reached the uterus. Arriving at the uterus, the only reason why a fertilized ovum rather than an unfertilized one becomes attached to the wall is that its cells (for there are many by this time) are hungry and possess the means of satisfying their hunger. The process of implantation is a continuation of the proteolysis by which it lays claim to its nutrient. Wherever the ovum happens to come in contact with the uterine mucosa after the fringe of follicle cells has been digested and absorbed it there adheres and soon dissolves a depression, and finally becomes imbedded, implanted. The mother reacts to protect herself against the invader, or, in modern phrase, to restrict the action of the enzymes. A balance is established, and the two organisms live in mutual tolerance, or as Bar has named it, "harmonious symbiosis."

When the placenta is finished the maternal blood is separated from fetal blood by the two-layered trophoderm and by certain mesoblastic structures, making an arrangement practically identical with that of the wall of an intestinal villus. Truly diffusible substances like glucose and urea readily pass the placenta (Morris and earlier workers), probably as readily as they pass the intestinal wall. Glucose arriving at the maternal placenta faster than it can be utilized by the fetus, is stored in the maternal side as glycogen until the last quarter of gestation when the fetal liver begins to assume its carbohydrate function, whereupon glycogen disappears gradually from the maternal placenta. The transfer of fat is still under investigation. Slemmons, in studying the lipoids in maternal and fetal bloods, has reached the conclusion that neither neutral fat nor cholesterol esters pass the placenta at all, but that cholesterol does. Since cholesterol is a colloid in the blood, proof that it passes the placental barrier is tantamount to proof that a selective activity is going on.

How proteins pass the placenta is the most important question of all. Amino-acids can readily find their way through the placenta (Morse). The question is where the indispensable building material is first modified. The weight of evidence is at present more in favor of a vitalistic conception of a placental function than of a mechanistic one.

The transport of iron from mother to fetus cannot be accounted for on mechanistic grounds. It seems certain that the fetus relies for this essential element on destruction in the placenta of the red cells of the mother's blood.

Under the mysterious guidance of the mechanism of heredity the proteins are built up into a new being which reproduces the essential characteristics of the phylum, class, order, genus and species to which the germ cells belong. Experiments lead to the conclusion (Heape-Castle) that a human child is born human not so much because it is

nourished by a human being as because the germ cells from which it came are human. It is not yet known just how closely related individual germ cells and the fostering mother must be related in order that development may proceed.

The demands of the fetus on the host for material for growth are very slight. Michel has shown that up to the end of the seventh lunar month not more than one-fourth of prenatal growth in terms of protein and salts has taken place. The total quantity of material needed for development up to the middle of pregnancy could be taken by the mother at a single meal.

That there is a negative nitrogen balance (output of nitrogen derivatives exceeds intake) in the early months of pregnancy is well known. The explanation is to be found in the means employed by the fetus for its nutrition at this stage, proleotytic destruction of the host (uterine mucosa, etc.). Products of proteolysis may well be the cause of "physiological vomiting." This activity is limited with the formation of the placenta and nitrogen retention becomes easier.

There then begins a retention of nitrogen that continues to the end of pregnancy and reaches such proportions that the total retention of nitrogen exceeds the requirements of the fetus, uterus, placenta, membranes and mammaries by a very considerable amount (Höffstrom-Wilson), an amount equivalent to the nitrogen in about 100 liters of milk. Accompanying this and associated with the removal of waste products from the fetus are changes in the urea, ammonia, creatinin, creatin, purin, and undetermined nitrogen, also in the inorganic sulphur, all of which (see many references) are to be explained on physiologic grounds.

A number of observers (Leimdorfer, Novak and Porges, Hesselbach) find a lower alveolar tension of carbon dioxid in pregnant women and state that it appears as early as the first estral cycle followng conception. Losee and Van Slyke confirm this for late pregnancy. It is part of a perfectly automatic respiratory regulation of the hydrogen-ion concentration and protects the host against acidosis.

During the puerperium a great readjustment takes place. Only the nitrogen balance has been studied in women during the involution period, but the same facts probably hold for sulphur, phosphorus, calcium, and magnesium. The chief source for the extra nitrogen found in the urine is the involuting uterus. The output reaches its maximum on the sixth or seventh day. A readjustment of the various nitrogen bodies occurs. There is no acidosis characteristic of the puerperium.

Collateral evidence points to a very great increase in the metabolism of the ovum from fertilization—a seven fold increase in the fertilized

urchin egg, rising rapidly to twenty-five fold. The scanty observation available on the developing fetus indicated plainly that the source of energy is carbohydrate, the most readily diffusible of all the foodstuffs. Studies on the new-born have already been reviewed.

Studies on women pregnant with a single fetus show an extra metabolism near term of about 4 per cent. over that of the same woman or other women in complete sexual rest. It is surmised that this is scarcely more than may be accounted for by the increased respiratory activity necessary to preserve the hydrogen-ion concentration of the mother's blood. The total product of conception, added to the mother's body, functions as so much maternal tissue—the high metabolism of the embryo being just counterbalanced by the inactive and relatively inactive structures.

Metabolism of Older Infant.—Talbot[23] points out that a careful review of the literature shows that there have been few instances in which an attempt has been made to obtain the twenty-four hour metabolism of infants. The fundamental experiments of Rubner and Heubner upon three normal infants stand out as giving the only twenty-four hour figures available. On the basis of these and other studies, Heubner maintains that an average normal infant requires per twenty-four hours 100 calories per kilogram of body weight during the first three months of life, 90 calories during the second three months, and 80 or less calories during the last half of the first year of life; and these figures are usually accepted as a basis from which to compute the energy requirements of normal infants.

Talbot utilized normal infants. The plan of observation was to have the infant inside the respiratory chamber as many hours out of the twenty-four as possible so that an accurate measure of the total respiratory exchange could be obtained. The infants were both breast fed and weighed 5.03 and 5.76 kg., respectively. Through intelligent cooperation of those in attendance it proved possible to reduce the time in which the infants were out of the respiratory chamber to one hour and twenty-nine minutes and fifty minutes, respectively.

On making due allowance for the time out of the chamber it was found that the total number of calories used by the infants was 70 and 74 calories per kilogram. What was measured was the actual heat produced by these infants. This represented the energy needs for basal metabolism plus the effect of muscular effort. Energy was of course lost in other ways, such as the potential energy of the urine and feces; this also must be supplied from the food. For the present this loss can only be estimated. Probably the greatest single

23. Talbot, F. B.: Twenty-Four Hour Metabolism of Two Normal Infants, with Special Reference to Total Energy Requirements of Infants. Am. Jour. Dis. Child., 1917, **14**, 25.

factor to be considered is the fat lost in the feces. This and the urea in the urine should not exceed presumably 15 per cent. of the total measured metabolism in a normal infant. When this has been added the child should remain in equilibrium, neither gaining nor losing. Something must be added for growth. If 20 per cent. is taken for the growth factor, it should give enough leeway for the infant to gain.

These figures, 15 and 20 per cent. added to the former figures, 74 and 70 calories, respectively, make a total food requirement of 100 calories per kilogram of body weight and 94 calories per kilogram of body weight, respectively.

The actual basal metabolism is represented by the total heat produced (74 and 70 calories) less the amount due to muscular activity —15 per cent. of the basal metabolism if the infant is very quiet, 25 per cent. if normally active, 40 per cent. if extremely active. An allowance of as much as 10 per cent. on one side or the other from the average figure of basal metabolism must be allowed for individual variation in infants. A sick baby has a higher "basal" metabolism because of increased restlessness, energy burnt up in fever, or impaired absorption of the food given him, one infant losing 20 per cent. of the food calories in the feces.

The metabolism of boys 12 and 14 years old—clinical calorimetry —has been studied by Olmstead, Barr and Du Bois.[24]

Hunger Phenomena.—The work of Carlson and Ginsberg on hunger contractions in the infant was referred to in this review two years ago.[25] Carlson and Ginsberg introduced a balloon and tube into the stomach of an infant and, using a manometer, secured graphic records of the stomach contractions. To the objection that the presence of the balloon in the stomach acts mechanically to produce gastric contractions, Carlson says definitely that it does not, and gives the following reasons: (1) the presence of the distended balloon in the stomach between the contraction periods does not induce these contractions; (2) in his gastric fistula case the gastric contraction could be observed directly through the fistula without any balloon in the stomach; (3) they come on just as frequently without any balloon in the stomach and produced the same effect (hunger); (4) in pigeons the periodic strong contractions of the empty crop can be seen directly through the skin and a balloon in the crop does not alter their frequency or intensity.

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24. Olmstead, W. H., Barr, D. P., and Du Bois, E. F.: Metabolism of Boys Twelve and Fourteen Years Old. Clinical Calorimetry. Arch. Int. Med., 1918, **21,** 621.

25. Holmes, James B.: Recent Advances in Anatomy, Physiology and Pathology of Childhood. Am. Jour. Dis. Child., 1916, **11,** p. 78.

Rood Taylor[26] has utilized a similar apparatus for the study of hunger phenomena in fifty-six infants varying in age from prematurity to 6 months of age, and also in a boy of 2 years with a surgically induced gastric fistula. The paper is a lengthy one. The following findings may be noted:

Confirmation of previous work that hunger contractions are greater in the new-born infant, and determination of still greater hunger contractions in the stomachs of prematurely born infants. Inhibition from the mouth is psychic in character and does not occur in young infants. Reflex inhibition from the presence of food in the stomach is present in infants of all ages; it may be only partially developed in young infants. In normally developing breast fed infants, hunger is not ordinarily an immediate cause for crying. In infants that are not well fed hunger contractions may occur before the stomach has been emptied, and consequently their presence is not in itself evidence that the stomach is ready for food. Hunger contractions may be present when the temperature (rectal) ranges between 104 and 105 F.

Taylor[27] has investigated also the appetite secretion of gastric juice in the infant. "There is apparently a gastric element in appetite. The contractions of the stomach institute hunger. Its profuse and rich secretion causes an entirely different sensation—not painful, but pleasant. This directs the flow of consciousness toward the matter of taking food." Much has been written regarding the presence or absence of this appetite or psychic secretion of gastric juice in the young infant. Taylor described an apparatus by which sham feeding can be carried out and gastric juice collected under conditions which give positive evidence of the amount secreted. He finds there is no appetite or psychic secretion of gastric juice in the young infant. Also that the empty stomach of the hungry infant secretes a gastric juice which is often as acid as that found in the adult's stomach—the more profuse the secretion the higher its acidity. He says that the secretion is not neutralized in the stomach, but flows out into the small intestine. Regurgitation through the infant's pylorus does not occur.

Allaria[28] points out that there are certain chemical and mechanical advantages of having the milk well mixed with saliva and estimates that the infant secretes an amount equal to from 10 to 20 per cent. of the ingested food. The tube fed infant may do without this in part, but there is no evidence that the gastric secretion is less than that of the actively nursing infant. "Therapeutic starvation in acute

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26. Taylor, Rood: Hunger in the Infant. Am. Jour. Dis. Child., 1917, **14,** 233.

27. Taylor, Rood: Hunger and Appetite Secretion of Gastric Juice in Infants' Stomachs. Am. Jour. Dis. Child., 1917. **14,** 258.

28. Allaria, G. B.: Jahrb. f. Kinderh., 1911, **74,** 252; ibid., Pediatria, 1911, **19,** 10. Cited by Taylor.

alimentary disorders and in summer diarrhea may owe its success in part to the heightened tonus of the alimentary tract, and in part to the pouring out of a highly acid detoxicating and disinfecting gastric juice into the small intestine."

Gerstley and Hoskins[29] have studied the effect of hunger on "nervous irritability" in dogs, as shown by the changes in the electrical excitability. Zybell in his clinical studies on spasmophilia concluded that any prolonged hunger aggravated the condition. Gerstley and Hoskins say that they carried out their examinations in the manner ordinarily employed in obtaining the reactions in children and that they found difficulty in obtaining any sort of definite standard. "In a normal dog, even at best, the reactions show extreme variability, changing not only from day to day but sometimes almost minute by minute." Other technical difficulties obtained. They failed to show any constant parallelism between the length of hunger and the degree of electrical irritability.

Malnutrition.—In a report by the Public Health Committee of the New York Academy of Medicine[30] malnutrition is defined as distinctly a pathologic entity, not a disease but a morbid physical condition. It may be symptomatic of disease or it may be the only evidence or result of defective metabolism or of complex and divers physiologic and environmental conditions. Whether caused by unsanitary surroundings, improper habits of life, lack of sleep and unsuitable food, or by poverty and disease, malnutrition is a social menace, as it hampers the natural development of functions of mind and body and predisposes its victims to a permanent life handicap. Every effort should be made to control it among children; its prevention is a distinct public health function.

Examination of New York school children has shown a yearly increasing per cent. of malnourished children. About 16 per cent. of the children are reported to need either supervision or medical treatment. Both the health department and the Association for Improving the Condition of the Poor consider 10 per cent. of the total number of school children an underestimation of the extent of malnourishment. In Philadelphia it was found in one section that 8 per cent. of the children came to school with no breakfast and 60 per cent. with what was considered an insufficient breakfast. It is clear that the problem is a great one.

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29. Gerstley, Jesse R., and Hoskins, R. G.: A Study of the Effect of Hunger on Nervous Irritability. Am. Jour. Dis. Child., 1917, **15,** 336.

30. Report of Public Health Committee of New York Academy of Medicine. Malnutrition Among Schoolchildren. Med. Rec., New York, 1918, **93,** 311.

In public discussions of malnutrition *poverty* is usually assigned the first place as a cause. Yet "however plausible the connection between low economic status and undernouishment may be, scientifically established proof is lacking of the causal relation between the two." Families having the same income and the same number of children vary greatly in their nutritional state. Ignorance and bad domestic management are potent factors. An English investigator found the causes in order of importance to be (1) influence and reaction of disease; (2) strong evidence of neglect, dirt or drink, and (3) defective feeding due to ignorance or poverty. Three per cent. of the children owed their condition to being pampered. The factor of housing cannot be dissociated from the accompanying conditions. These may all be called extrinsic causes.

Intrinsic causes include such debilitating factors as chronic absorption from diseased tonsils, decayed teeth, or obstructed nasal breathing, things that can be remedied, as can also some of the respiratory or digestive disturbances. The agencies that are available for combating the conditions are:

(*a*) Clinics for malnourished children—(see report of one as given later).
(*b*) Fresh air classes—maintained primarily to combat tuberculosis; providing of meals given up because of the high cost and discovery that many patients neglected to provide children with breakfast when meal would be given at school.
(*c*) Tuberculosis preventatorium—where children of tuberculous diatheses are kept six months and given medical, educational, and institutional care of high order.
(*d*) School lunches—dealt with more fully later.
(*e*) Baby welfare stations—demonstrations of cooking cereal, and how best to expend a dollar for cereals; practical instruction in other cooking.
(*f*) Diet kitchen—opened in connection with settlement houses and the like.
(*g*) Fresh air funds—providing camps; need of better supervision of rest and diet, and need of longer stay for many children.
(*h*) Education—in some sections more necessary among native born parents than among foreign born (Mauny).

School Lunches.—A considerable part of the report is devoted to a consideration of the "school lunch." The practice of feeding children at school, we are told, is not a new venture in the educational world. It has been known in Germany since the end of the eighteenth century, and it was introduced in France in 1849, and in England in 1866. The difficulty of instructing children who suffer from malnutrition has been recognized by schoolmasters, and arrangements have been made to provide gratuitous meals at school, paid for from the public funds. In America the practice has been different in that it is recognized that many children, even those of the very poor, bring several coppers with them to spend during recess, usually for candy and indigestible articles. These same pennies can buy wholesome and nutritious food at the school, if the same is properly organized.

Indigent children may receive meal tickets from the teachers, the cost being covered by a special fund.

The experience of Philadelphia is reviewed at some length. A five years' experience fully established the fact that "children will buy wholesome food at school if given the opportunity," and that the service can be put on an almost self-supporting basis. It was found that 66 per cent. of the expense was for food, 32 per cent. for supervision and wages, and 2 per cent. for repairs and replacing of equipment. In New York where lunch service is maintained in thirty-five elementary schools, it is found that about one-fifth of the children avail themselves of the lunches. The money paid by them covers only the cost of the food.

The food served to the children is examined as to quality and prepared under carefully supervised sanitary conditions. The menus are prepared by a trained dietitian; they must not offend religious or racial prejudices, nor fall below a desired standard of food value; the proper balance of constituents must be maintained. The children are free to select the foods, but all must buy a bowl of soup before anything else can be obtained.

In Table 2 are shown some of the combinations of food that the children were able to purchase several years ago at a cost of three cents. The same combinations now cost six cents.

TABLE 2.—Food Combinations for School Lunches

	Calories Per Portion		Calories Per Portion
Green pea soup	128.31	Vegetable soup	85.00
Bread, 2 slices	200.00	Egg sandwich	236.00
Apple sauce	108.57	Rice pudding	108.76
	436.88		429.76
Cream of barley	120.47	Clam chowder	82.00
Cheese sandwich	250.17	Butter sandwich	247.25
Chocolate pudding	101.50	Jelly tarts	83.85
	472.14		413.10
Macaroni and tomato	105.29	Bean soup	111.27
Apple jelly sandwich	240.17	Bread, 2 slices	200.00
Cocoa	100.00	Prunes	180.00
	445.46		491.27

The committee makes numerous recommendations directed chiefly toward dissemination of knowledge of proper nutrition and practical cooking, and improvement of children's lunches and the conditions under which they are eaten. They recommend that school lunches be extended. If private means were not available to assume the desired extension, it should be taken over by the municipality.

Classes for Undernourished.—Smith[31] reports his experience with a class of 188 undernourished children drawn from the poorest class of dispensary patients (New York City). No child was admitted to the class unless he was 5 pounds or more under weight for his age. The children returned at intervals of one week to a month. At least one visit was made to each home, and the cases were followed up as far as one social worker could do this. Some adult member of the family was required to come with the child for the first few visits.

A fairly complete history was made on admission to the class, with particular attention to those facts that bear most directly on malnutrition. The social worker checked up the data and added other facts. The general plan was to make a careful diagnosis, to correct remediable physical defects, to determine and correct any economic factors that had a bearing on the case, and to try to improve the diet and hygiene of the child by every possible means.

The child's daily life was gone over with the attendant. If decayed teeth were present the child was referred to or taken to a dentist. If tonsils or adenoids were giving symptoms (or if they were much enlarged) operation was advised, provided the child's general condition warranted it.

A printed diet list was provided. The first lists used were simply ideal diets for a child, but it was found the expensive foods occupied the most prominent place in the lists. The lists were then rewritten several times, until finally a somewhat unique form was adopted. This contains six columns. In the first three are indicated (1) the meal and the dishes stated in general terms; (2) the quantities of each dish; (3) simple directions for cooking. In the next three columns are indicated (1) the cheaper article of food that may form the dishes, (2) the more expensive, (3) the most expensive. Expensive is here used to mean low nutritive value in proportion to price paid—for example, corn flakes, puffed rice, etc. Rules for eating are attached. Also a list of forbidden articles.

A food exhibit was provided. It was based on the day's total ration. Three meals were laid out each day, and each consisted of suitable dishes in proper amount. The visual impression made on the mother and child was found to add tremendously to the significance of the printed list of foods in the diet list. The imitations were so real that nearly everyone was deceived at first glance.

Class talks were given frequently. Weekly return visits were sought. A photograph of each child was attached to the history. They aroused the interest of the children in the class and later ones

31. Smith, Charles Hendee: Methods Used in a Class for Undernourished Children. Am. Jour. Dis. Child., 1918, **15,** 373.

were useful in showing improvement. They were made inexpensively by lining up several children for one exposure with a cheap camera and then cutting up the finished print.

By use of these methods it was found possible, even among the poorest class of dispensary patients, to make 57 per cent. of the children gain at 1.7 times the average rate for their ages, and 22 per cent. at about the average rate. In the remaining 21 per cent. there was in every case one or more easily ascertainable reasons for the failure—among the significant facts were: low family income (?); failure of mother ever to attend class, a markedly positive von Pirquet reaction, inability of mother to speak English. "It seems fair to conclude that the class method is of value in the treatment of undernourished children even when they must be handled in large numbers."

Rations for boys' military training camps has been made a subject of study by Fitch.[32]

Miscellaneous.—Hess and Unger[33] have investigated the diet of negro mothers in New York City. They selected a district with a population of about 9,000, composed almost entirely of negroes. It was found that the diet as a rule afforded ample calories, but that it was not well balanced. There was an excess in the intake of protein (beef, cooked very frequently as stew), adequate carbohydrate, and a deficiency of about 25 per cent. of the fat in the dietary. There was a preponderance of canned and dried vegetables, fresh vegetables being taken on the average but once a week, and fresh fruit about twice a week. The dietaries were thus deficient in fat and in calcium and other salts, for which we depend largely upon milk, vegetables and fruits. Since the majority of the negroes came from the West Indies, St. Kitts, the Barbadoes, and St. Croix, where they were accustomed to a diet consisting mainly of fresh vegetables and fruits and where rickets is practically unknown, Hess and Unger argue that the change to a deficient dietary in the mothers may be largely causative of the striking amount of rickets in their offspring.

Chapin[34] calls attention again to the heavy morbidity and mortality that exist among neglected and abandoned infants. There are but two plans for handling these children: they can either be boarded out or collected in institutions. After reviewing the results obtained by representative institutions and contrasting their work with the figures obtainable where babies are boarded out and properly super-

32. Fitch, W. E.: Rations for Boys' Military Training Camps. Military Surgeon, 1917, **40,** 518.

33. Hess, A. F., and Unger, L. J.: Diet of the Negro Mother in New York City. Jour. Am. Med. Assn., 1918, **70,** 900.

34. Chapin, Henry Dwight: Systematized Boarding Out vs. Institutional Care of Infants and Young Children. New York Med. Jour., 1917, **105,** 1009.

vised, Chapin concluded that the home, though poor and imperfect, is better in the long run for the little child than the institution.

Two factors militate in favor of a high death rate in institutions: (1) lack of individual care, and (2) lack of fresh air. Cross infections from ordinary colds, influenzas and respiratory diseases are always liable to be dangerous where many individuals are crowded together; epidemics are frequent. The child contracts disease because it is in an institution.

By boarding out the danger of spreading communicable diseases are reduced to a minimum. By no other known method of handling can so many children of this type be cared for with so little spread of infection (data from the Speedwell Society, Morristown, N. J.). Children in a boarding home if they do not succumb to actual disease are usually as strong as other children in the family; infants who are retained very long in institutions are not apt to be vigorous. Chapin says:

> Boarding, if properly employed, will not only give better results, but is cheaper in operation. To the money locked up in the original cost of the plant must be added the cost of operation and the amount of taxes remitted; all this enters into the real expense of the work done by them. In boarding out, the money goes into aiding the upkeep of normal homes. The constant oversight of doctor and nurse helps each foster mother in the care of her own children. The general standard of living may also be raised.

Bateman,[35] writing from the Sheffield Laboratory of Physiological Chemistry (Yale University), points out that evidence has been accumulating during the past fifteen years which shows that raw egg-white occupies an exceptional position among native foodstuffs. He reviews this evidence. It is shown that native egg-white offers serious obstacles to digestion. This is an important matter, for raw eggs and egg-white (egg albumin) have enjoyed a great vogue as the mainstay of various diets, especially for the sick. Certain recent writings have served to support this use, but Bateman shows that they rest on mistaken assumptions. He feels that his study shows that the current reasons for using raw egg-white are not well suppported, and indicates that use of raw egg-white is decidedly inadvisable. "A substance which fails to stimulate a flow of gastric juice and is antipeptic, which hurries from the stomach, calls forth no flow of bile, and strongly resists the action of trypsin, which is poorly utilized and may cause diarrhea has evidently little to recommend it as a foodstuff of preference for the sound person, let alone for the invalid."

Raw egg can be made digestible by heating it at 70 F., by incubation with dilute acids and alkalis at 37 C., by precipitation with

35. Bateman, W. G.: The Use of Raw Egg in Practical Dietetics. Am. Jour. Med. Sc., 1917, **63,** 841.

alcohol, chloroform, or ether; by partial digestion with pepsin, and by conversion into alkali metaprotein.

Lack of space forbids more than a passing reference to the studies on the digestibility of the so-called war-breads,[36] Victory bread, etc.

Pease and Rose[37] have carefully studied the banana from a nutritional point of view. This fruit has been regarded as of doubtful value in the dietary of children. Its chief food constituents are the carbohydrates, which amount to about 22 per cent. In the green fruit these are in the form of a starch, but as the fruit ripens this is converted into, first, sucrose and finally into invert sugar. The protein content (less than 1 per cent.) is of unknown nature; the fat and fiber are negligible. The ash is important, being similar to that of other common fruits. Vitamins are doubtless present in fair share. When fully ripe, banana is apparently a good fruit for children, provided it does not crowd out other foods more essential for growth. It may for a time replace cereals and potatoes, in part. The *underripe uncooked* fruit should never be given to children.

The banana is fully ripe when the peel takes on a golden yellow and begins to be speckled with brown. It finally becomes brown all over and is then still edible provided the cover is still intact and the pulp shows no signs of fermentation. (The brown color of ripening must not be confused with the brown patches due to bruising.)

An adult receiving a diet of 1,000 gm. banana, 1 quart of milk and 1 cup of sweetened coffee daily for a week experienced comfort, satisfaction and unimpaired efficiency. The utilization of the banana carbohydrates in this and similar cases was 98.8 per cent. In the experiments on children the banana was introduced as a substitute for the more starchy foods such as cereals and potato, and ranged in amount from one small banana to three-quarters of the day's carbohydrate quota. They were mashed to prevent bolting an unmasticated lump. The stools were examined for signs of fermentation and analyzed for the presence of starch and dextrins.

The nutritive value of the banana is relatively high, approximately 1 calorie per gram of pulp; and its carbohydrates appear to be not less assimilable than those of cereals and potatoes. In the raw fruit the digestibility is directly proportional to the ripeness of the fruit—conversion of starch to sugars. There is no positive evidence that the banana influences bowel movements. Prolonged use of the under-

36. Spriggs, E. I., and Weir, A. B.: Digestibility of Bread Made from Two Parts of Wheat and One Part of Oats, Barley, Maize, or Rice. Lancet, London, 1917, **2,** 724 (for example).

37. Pease, Marshall, and Rose, Anton R.: The Banana as a Food for Children. Am. Jour. Dis. Child., 1917, **14,** 379.

ripe fruit produced undesirable symptoms. Baked bananas both from the green and early yellow stage were well utilized.

Meyers and Rose found that larger amounts of the sugars could be given in the form of bananas than as pure sugars without causing digestive disturbances. From a number of observations it seemed that the banana was a specially valuable form of food in the dietetic treatment of cases of nephritis with nitrogen retention. As the ash is alkaline, it might have some value in combating a tendency to acidosis.

Bosworth, Bowditch and Giblin,[38] working in a school where it is customary to feed topmilk formulas, state that it is well recognized that the digestion and absorption or nonabsorption of fats is probably a source of the greater part of the trouble in feeding cow's milk modifications. This difficulty they believe lies not so much in the fat itself as in the accompanying inorganic constituents of cow's milk dilutions. Cow's milk is especially rich in calcium and phosphoric acid, substances which the young of the cow use to develop rapidly growing bone tissue, but which the infant uses very sparingly. The excess is eliminated by the infant in the feces as insoluble calcium phosphate and calcium soaps. While this mode of eliminating the excess calcium present in the cow's milk is in one way a protection to the infant, in that it prevents the calcium from entering the body fluids and tissue in organic combination, subsequently to set up a toxic condition (unpublished work from their laboratory) it may, on the other hand, bring about marked nutritional disturbances.

The examination of many stools from bottle-fed infants has led them to believe that although neutral fat, free fatty acids and soaps may all be found in these stools, the appearance of neutral fat and fatty acids, except in the case of diarrhea, are wholly secondary, being due to a faulty feeding which allows an excessive amount of calcium, available for soap formation, to enter the intestines. There the conditions are very favorable for the formation of insoluble calcium salts, which, as they are precipitated, may carry down with them by occlusion both neutral fat and free fatty acid. Data submitted are to show that the soaps present in the stools of bottle-fed infants receiving modified milk (containing 2 to 3 per cent. fat) are almost wholly insoluble soaps, and, as calcium is the only insoluble base present in appreciable amount, it is concluded that the insoluble soaps are calcium soaps.

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38. Bosworth, A. W., Bowditch, H. I., and Giblin, Louise A. (Boston): Studies of Infant Feeding. X. The Digestion and Absorption of Fats. 1. Calcium in Its Relation to the Absorption of Fatty Acids. Am. Jour. Dis. Child., 1918, **15,** 397.

In order that the soaps formed from the fatty acids which are produced by the digestion of fats may be assimilated, it is necessary that they be absorbed and pass through the intestinal wall into the body fluids. To be thus absorbed they must be soluble in the intestinal juices, or more definitely speaking, in the bile. A study of the solubility of calcium soaps in bile, while not yet complete and rather inconclusive, is thought to indicate that calcium oleate shows a higher degree of solubility in bile at 37 C. than do the calcium soaps of stearic, palmitic or myristic acids. This, if true, would explain the preponderance of the calcium soap of palmitic acid over other soaps present in infants' stools.

The influence of the kind of calcium salts present in the food on the amount of calcium soaps eliminated from the stools was studied by feeding synthetic (calcium free) food to which various salts of calcium were added (dicalcium phosphate, calcium caseinate, and calcium caseinate and acetate). In this connection it is pointed out that it is not the mere presence of calcium salts in the food which determines the presence of calcium soap in the stool, for other factors enter in, such as the forms in which the calcium is present in the food, bacterial activity within the intestines, and the amount of hydrochloric acid secreted into the stomach, since this may change the forms of calcium compounds.

Having been led by their investigations to believe that many of the troubles encountered with bottle-fed infants receiving cow's milk must be attributed to the ill effects produced by the calcium in cow's milk, Bosworth, Bowditch and Giblin have perfected a method for "reconstructing" cow's milk which permits them to remove nearly all the calcium from the original milk. Inorganic phosphorus and calcium are then added in desired amounts. In other words, not only are the percentage of protein, fat, and sugar varied as needed, but an attempt is made also to properly balance the mineral elements of the food.

This work is in line with the tendency to pay increasing attention to the mineral elements of food.

Hess and Unger[33] present work to show that so far as the colored race is concerned, the development of rachitis is based on some dietetic insufficiency which appears to be satisfied by the administration of cod liver oil. Because rickets is a predisposing cause of respiratory diseases, such as pneumonia, bronchitis and possibly whooping cough and tuberculosis, the successful prevention of rachitis among infants would tend to reduce infant mortality.

The fact that breast fed children fall victims to this deficiency disease suggests that probably the dietary of the mother lacks a certain

required protective substance, as for example, is the case among mothers in the Philippines, where children develop beriberi. Cow's milk in itself does not always seem to supply the deficiency; and inferior grades of condensed milk and proprietary infant foods more frequently fail.

Hess and Unger think it possible that cod liver oil may prove as prophylactic against rickets as orange juice is against scurvy. If so, it should be supplied at cost in baby stations and its use taught generally.

Hess[39] holds that a faulty diet is only one of the several factors in the pathogenesis of infantile scurvy. In a recent study (1917) it has appeared to him that pasteurized milk is a contributory cause if it is not fresh—i. e., if given twenty-four to forty-eight hours after pasteurization. From this point of view milk pasteurized in the city is preferable to milk pasteurized at the creamery, which reaches the consumer much longer after the heating process. Ageing seemed to have a greater rôle in the production of scurvy than heating, whether the milk was pasteurized or raised to the boiling point. It was found (Hess) that even raw milk on ageing loses its antiscorbutic properties. However, infantile scurvy is not, he believes, a simple dietary disease, but rather one due to faults in the diet allowing the intestinal bacteria to elaborate toxins; that is, an intestinal intoxication or an auto-intoxication due to the overgrowth of harmful bacteria, the product of an unbalanced flora, which is no longer controlled by a proper dietary. As the toxin may not always be the same, the question is raised whether from a strictly etiologic standpoint the disorder should be regarded as an entity.

Oliguria is a common symptom of scurvy. Hess thinks the mild therapeutic effect of citric acid may be ascribed partly to its diuretic properties. Orange juice is found also to bring about marked diuresis.

Some hemorrhages that occur are to be regarded as scorbutic; others are due possibly to the susceptibility to infection (furunculosis, nasal diphtheria, "grippe," etc.) that is an important and striking symptom of scurvy (Hess), and are to be regarded rather as focal complications.

When scurvy is latent among a number of infants and an infectious disease (such as "grippe") is suggested, scurvy may appear in epidemic form.

Torrey and Hess[40] revert to the question that has been raised as

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39. Hess, Alfred F.: Infantile Scurvy. V. A Study of Its Pathogenesis. Am. Jour. Dis. Child., 1917, **14**, 337.

40. Torrey, J. C., and Hess, A. F.: The Relation of the Intestinal Flora to the Scurvy of Guinea-Pigs and of Infants. Proc. Soc. Exper. Biol. and Med., 1918, **15**, 74.

to whether scurvy in guinea-pigs and in human beings is due to constipation and to the putrefactive activity of the bacteria in the intestinal tract. They studied the intestinal flora of guinea-pigs on diet that led to the development of scurvy, and diets containing antiscorbutic properties that cured the same. They found no change in flora on adding orange juice to the diet. It seemed that the development of scurvy was not associated with an overgrowth of putrefactive bacteria. (The actual amount of putrefaction present, however, can only be determined by a chemical study, and this was not made.)

Holt, Courtney, and Fales[41] report on the effect of administering cod liver oil to an 8½ year old girl who weighed but 29 pounds, and was of the height of an average child of 3 years. A tentative diagnosis of infantilism of intestinal origin had been made. There were but slight evidences of old rickets and none whatever of active rickets. During ten months of improved digestion (from the omission of certain disturbing articles of food) and an enlarged diet, particularly the addition of milk, cod liver oil, and a preparation of malt in which it was administered, the child grew 2 inches in height and gained 9½ pounds in weight.

The cod liver oil was administered with the hope that it might influence salt retention. At the same time, by increasing the diet, especially the amount of milk, an attempt was made to increase the salt intake. Careful metabolic studies were made. The most striking changes that occurred under the treatment were in the salt balances. Instead of negative balance in total ash of 6.77 per cent., a positive balance of 14.3 per cent. is shown. All the salts showed positive balances. The most marked change was in the calcium.

The results in this case, which far exceeded the expectations, are thought to show conclusively how essential to proper growth is assimilation of the salts ingested. In this instance the most important factor is thought to have been the cod liver oil, the next being the milk.

Phosphorus.—Phemister[42] contributes an article on the effect of phosphorus on growing normal and diseased bones. Since the experimental work of Wegner[43] phosphorus has been used more or less extensively as a therapeutic agent in disorders of ossification. Wegner administered 1/400 grain of yellow phosphorus daily to young growing dogs, cats and chickens over considerable periods of time and observed definite changes in the bones, both in the diaphysis and epiphysis.

41. Holt, L. E., Courtney, A. M., and Fales, H. L.: Effect of Cod Liver Oil on Growth in Case of Intestinal Infantilism. Am. Jour. Dis. Child., 1917, **14,** 222.

42. Phemister, D. B.: The Effect of Phosphorus on Growing, Normal and Diseased Bones. Jour. Am. Med. Assn., 1918, **70,** 1737.

43. Wegner: Virchows Arch. f. path. Anat., 1872, **55,** 9.

Adult bones were not affected. In fractures the formation and ossification of callous was stimulated. Kassowitz[44] repeated and confirmed Wegner's experiments and brought out the additional fact that from two to four times the dose of phosphorus that produces osteosclerosis, leads to osteoporosis. Kissell's[45] negative results were perhaps thus to be explained. Miwa and Stoeltzner[46] were able to confirm Wegner's findings in a few of their experiments, and Stoeltzner, as a result of extensive clinical experience, became a firm advocate of phosphorus therapy in rickets.

The effect of administering cod liver oil and phosphorus in increasing the calcium and phosphorus retention in rickets has been known for some years. Schabad[47] has maintained that phosphorus when administered alone in the usual therapeutic doses causes no increase in calcium accumulation in the body, and in some cases studied even accelerated its elimination. Cod liver oil caused a moderate increase, while cod liver oil and phosphorus caused a marked increase in calcium accumulation. Cod liver oil is apparently not, as some have thought, merely a convenient vehicle for phosphorus. Lime salts, especially calcium lactate, when given with cod liver oil and phosphorus, increase still further the calcium accumulation. Schabad concludes that the cod liver oil, not the phosphorus, is the primary active substance, and that the phosphorus acts secondarily by augmenting the accumulation that is started by the oil. (Schloss[48] questions the value of phosphorus in the combination; then in a later communication states that calcium phosphorus preparations alone, when given with breast feeding, are almost as effective in improving the calcium and phosphorus balances as when they are used with cod liver oil. He concludes that the nature of the food and the condition of absorption in the body are of more importance than the form of salt addition.)

Phemister points out that as 98 per cent. of the calcium of the body is stored up in the bones, they should show a variation in calcium content in case of an increase or decrease in the amount retained in the body; that this can be determined either by studies at necropsy or by roentgen studies of the bones of the living; that no evidence of either kind is offered by Schabad or Schloss in support of their claims. Hence the interest of his paper, which is fully illustrated with roentgenograms. His findings indicate that phosphorus (here given alone, and continued in one instance as long as eight months) affects the

44. Kassowitz: Ztschr. f. klin. Med., 1884, **7.**
45. Kissell: Virchows Arch. f. path. Anat., 1896, **144.**
46. Miwa and Stoeltzner: Jahrb. f. kinderh., 1898, **57.**
47. Schabad: Ztschr. f. klin. Med., 1909, **57,** 454; 1909, **58,** 94; 1910, **59,** 435; Jahrb. f. Kinderh., 1910, **72,** 1.
48. Schloss, Ernst: Jahrb. f. Kinderh., 1913, **28,** 694 (cit. from Holt).

bones of normal children in much the same way as described by Wegner for experimental animals. The effect on enchondral bone is especially well marked. Also there is for some time after the phosphorus is stopped a continued but less well marked overproduction of bone in the juxta-epiphyseal region of the shaft that is probably due either to the cumulative effect of the phosphorus or to the stimulating influence of the excessive stores of calcium salts in the neighboring bone.

Judging from the general effect it produces, phosphorus if given early in fractures during the active period of repair should stimulate callous formation and ossification. "In nonunion, however, when the natural reparative impulses have been exhausted, little should be expected from its use." In rickets, during the florid stage, "the bony tissues have lost the power of depositing lime salts, and as phosphorus is presumably unable to restore the power, no appreciable effect from its administration would be detectable by means of the roentgen ray, although it may increase the amount of osteoid tissue formed."

Studies like the above labor under the difficulty of getting plates that in exposure, development, etc., are really comparable. Phemister's work is of interest in showing that phosphorus when given alone may have a marked stimulating effect on bone production in the zones of normal growth, and in contradicting the views of Schabad relative to calcium metabolism in healthy children.

Dicalcium Phosphate.—Bowditch and Bosworth[49] have carried out studies to show whether the dicalcium phosphate ($CaHPO_4$), which is present in cow's milk to the extent of 0.175 per cent., is available as food. They conclude that it is not available to children under 4 months of age and only partly available to older children. They hold that the utilization of calcium phosphate by the older children is probably dependent on the more abundant secretion of hydrochloric acid. In calculating the amount of mineral elements present in modified cow's milk for use in infant feeding, they would consider the dicalcium phosphate as unavailable and make a corresponding reduction from the total mineral elements in milk. It is possible to render the urine phosphorus-free by feeding sufficient soluble calcium to precipitate the phosphorus of the food as insoluble calcium phosphate.

"Vitamin."—McCollum and Simmonds[50] say that it has become evident that among the thousand or more chemical substances which occur in animal and plant tissues it is essential only that the diet of the mam-

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49. Bowditch, H. I., and Bosworth, A. W.: Availability of Dicalcium Phosphate When Present as a Constituent of Infant's Food. Boston Med. and Surg. Jour., 1917, **177,** 864.

50. McCollum, E. V., and Simmonds, N.: The Nursing Mother as Factor of Safety in the Nutrition of the Young. Am. Jour. Physiol., 1918, **46,** 275.

mal shall contain the following: Sixteen or seventeen amino-acids which result from the digestion of the complete proteins; the carbohydrate glucose or one of its polysaccharids (starch, dextrin, etc., or other sugar which in the body is convertible into glucose); probably nine inorganic elements in the form of suitable compounds (Ca; Mg; Na, K, Cl, P., I. Fe, S), and two as yet chemically unidentified dietary essentials, fat-soluble A, and water-soluble B.

Lack of certain of these substances leads to disease (beriberi, for example, or (Funk) scurvy and pellagra), or apparent mere lack of growth. This may be studied in animals.

Young animals, for example, cannot grow when fed a single seed or a mixture of seeds even though the latter be supplemented with purified protein and a fat containing fat-soluble A. The inorganic factor is the first limiting factor, and sodium, chlorin and calcium must be added before growth becomes possible.

The extent to which the maternal organism through the secretion of the mammary gland can serve as a factor of safety for the suckling is still very little understood. Examples of the exercise of a synthetic function by the mammary tissue are seen. There is evidence also of variability of the milk depending on the composition of the mother's food. Indeed, the quality of the milk as judged by its growth producing power is dependent in a surprising degree on the quality of the diet of the mother. McCollum and Simmonds' studies on rats confirm and explain Andrew's[51] studies on human milk, "and establish the fact that milk production may take place under dietary conditions such that the product is deficient in certain complexes necessary for growth."

The nursing mother, then, does act as "a very important factor for her young in that her mammary tissues can remove from the blood all elements necessary for the production of milk, approximately more nearly the normal in quality than was the food from which it was produced."

Fischer[52] writes in a nontechnical manner on the subject of vitamins and recent literature pertaining to their application in infant feeding.

Roper and Eddy[53] in presenting a study of the use of "pancreatic vitamin" in cases of marasmus refer to Casimir Funk's isolation of "vitamin" from rice polishings, in 1911, and later from yeast and other sources; Mendel and Osborne's recognition of certain substances

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51. Andrews (Philippine Jour. Sc., Series B, 1912, **7,** 67) induced Philippine women whose infants had just died of beriberi, to nurse young puppies. These in all cases developed paralysis of the posterior extremities, which is one of the characteristic symptoms of the disease.

52. Fischer, L.: Recent Literature Pertaining to Vitamins: Their Application in Infant Feeding. Med. Rec., New York, 1917, **92,** 13.

53. Roper, J. C., and Eddy, W. H.: Use of Pancreatic Vitamin in Cases of Marasmus. Am. Jour. Dis. Child., 1917, **14,** 189.

found in butter fat as necessary for growing rats, and McCollum's grouping of the two as (1) fat-soluble A (his name for Mendel's butter fat factor), and (2) water-soluble B (his name for Funk's "vitamin"). McCollum has suggested that the name vitamin be dropped altogether.

All attempts to purify or isolate these substances further have failed. Any chemical test for their presence is lacking. According to Roper and Eddy we have at present only two ways of determing their presence in a given diet or substance, namely, by producing polyneuritic conditions in pigeons through feeding of polished rice and then treating the birds with the "vitamin"-containing substance, or by feeding rats on a maintenance diet and then by the addition of the vitamin to the diet noting the improved tendency of the growth curve as a result. The agent or substance that prevents polyneuritis may not be the same as that which prevents growth. Orange juice, for example, which contains something that prevents scurvy, does not promote growth.

Seidell having shown that the active substances can be obtained from their crude solutions without loss of strength through shaking them with a special form of fuller's earth, Lloyd's reagent, which has the power of absorbing them, Eddy and Roper utilized Lloyd's reagent to prepare a powder from an acid alcoholic extract of minced lambs' pancreas, such that 1 gm. of the powder contained "the vitamin of 54 gm. of pancreas." The efficiency of the preparation in growth stimulation was demonstrated in white rats. They administered it to ten infants, six of which were cases of marasmus. Observations on a typical marasmic infant seemed to show that the preparation had a definite growth-producing effect. Control studies on rats showed the cereal and condensed milk diet which the infant was receiving was markedly lacking in natural vitamins, and that the addition of pancreatic vitamin to such a diet was sufficient to convert it into an efficient growth-producing diet. Five other infants offered further evidence for the same conclusions. In all five cases the infants gave every indication of marked improvement physically. In three other infants suffering from malnutrition, growth had already begun when the extract was added to the diet, and the effect was not so clearly demonstrable.

Eddy and Roper think the use of "pancreatic vitamin" seems to offer definite hope of success as an agent for stimulating the growth of marasmic children. Hess has shown a similar effect from yeast. The dosage is not yet satisfactorily worked out, and the conditions under which the effect is produced are not yet defined.

(Emmett and McKim[54] from studies on pigeons conclude "that

54. Emmet, A. D., and McKim, L. H.: The Value of the Yeast Vitamin Fraction as a Supplement to a Rice Diet. Jour. Biol. Chem., 1917, **32**, 3.

there are apparently two so-called vitamins associated with rice polishings, one of which cures polyneuritis and one of which produces weight, and of these two, the Seidell yeast vitamin preparation (prepared with Lloyd's reagent) contains chiefly the curative fraction, along with a small percentage of the other." Funck found Seidell's vitamin preparation from autolyzed yeast with Lloyd's reagent was greatly deficient in the growth stimulant and had lost some of its antiscorbutic power.)

Gerstenberger,[55] in a lengthy article, covers much recent literature on scurvy and offers an hypothesis regarding its pathogenesis. He imagines that all the symptoms of scurvy as we know them today (hemorrhage into the bones and tissues, rarefaction and swelling of the osseous system, exaggerated reflexes, tachycardia and dilatation of the heart, and hyperesthesia) may be explained "on the common basis of a primary or secondary interference with one or more of the normal functions of calcium, alone or in conjunction with its physiologic anion, a condition which he is pleased to call *a partial defunctioning of calcium and its physiologic anion;* that in scurvy as we see it occur in infants this defunctioning is caused by a substance produced through a break in the metabolism of carbohydrates, whatever their original source may be; that the break occurs as the result of the absence or inactivity or relative insufficiency or inadequacy of some physiochemical substance or "vitamin" essential to the establishment and performance of normal carbohydrate metabolism; that the defunctioning substance possibly is oxalic acid or some other agent that has a similarly strong affinity for calcium, and that after combining with calcium is soluble with similarly great difficulty.

Comby[56] calls attention to the injurious effects on infants of a diet that is low in butter fat. This has become an important matter owing to the diminished fat ration of warring peoples. The effect of giving too much fat in the diet of infants is the production of colic, vomiting, and diarrhea, as is well known. A diet that is continuously too low in fat may lead to two forms of disturbance, a general one which is termed by Comby *dystrophie adipogénétique,* and a local one attacking the eye, *xérophthalmie.* The latter is often the local manifestation of a more general condition. C. E. Bloch[57] (Denmark) has recently described 40 cases of xerophthalmia. Dryness and wrinkling of the conjunctivae is the first noted, then the appearance of bluish white spots that give the name xerosis. The affection progresses, the con-

55. Gerstenberger: Pathogenesis of Infantile Scurvy: An Hypothesis. Am. Jour. Med. Sc., 1918, **155,** 253.

56. Comby, J.: La diete maigre chez les nourrissons. Arch. de méd. d. enf., 1918, **21,** 313.

57. Bloch, C. E.: Cited by Comby, note 56.

junctiva becomes insensible; necrosis sets in. In other cases the activity of the process is shown by the appearance of dacryorrhea and photophobia.

The more general affection assumes three forms: (1) a general atrophy, athrepsia; (2) a dystrophic form, and (3), in children of a year or more, a universal dystrophic process in which the volume corresponds to the age and there is no abdominal distention but there is excess pallor and considerable emaciation. The cutaneous surfaces may be white and dry, and exhibit dermatitis.

These conditions have long been known in Japan, where they have been attributed to the use of a dietary that is deficient in fat, and treated by administering cod liver oil. Mori[58] described the condition under the name of *hickan* and has given statistics on many cases (1899-1904).

Reaction of Mouth.—The power of the saliva to maintain a protective function over the teeth against dental caries has been long a subject of investigation but little has been proved. Miller, in 1891, attributed a strong alkaline reaction to the animal saliva and a great content of carbonate of the alkalies that might neutralize acids, thus tending to prevent the appearance of caries. Marshall, in 1915, stated that saliva is amphoteric, and that therefore for it to be a factor in protecting the teeth it must neutralize either acid or alkaline substance as taken into the mouth, and that it is the degree of this power to maintain a neutrality in the mouth which is indicative of susceptibility to caries. Gies and co-workers could not substantiate this.

Howe and Keniston[59] have sought to find out what relation there may be between the salivary factor of Marshall and the incidence of dental caries. The work is from the laboratory of the Forsyth Dental Infirmary for Children, in Boston. They find that the saliva of persons immune to dental caries varies, as does that of persons with carious teeth. Their tables do not show consistently that as the difference between the total neutralizing power of resting and activated saliva diminish, liability to incidence of caries increases. There is doubt as to the importance of the salivary factor.

Rongel[60] has studied the modification of the mouth reaction in infants on different diets.

Air Swallowing.—In a lengthy article Kantor[61] points out that, although the symptoms associated with gas in the digestive tract—

58. Mori: Cited by Comby.

59. Howe, Percy R., and Keniston, Mildred R.: The Salivary Factor in Relation to Dental Caries. Am. Jour. Physiol., 1918, **46,** 28.

60. Rongel: Arch. de méd. d. enf., 1918, **21,** 27.

61. Kantor, John L.: A Study of Atmospheric Air in the Upper Digestive Tract. Am. Jour. Med. Sc., 1918, **155,** 829.

belching, tympany, ameteorism, flatulence, etc.—have been the subject of comment from earliest times, it has most commonly been taken for granted that the gases in question have their origin entirely within the body, whether from the decomposition of food, exhalation of vapors, or from the interplay of gas-producing juices. He reviews the general historical background of the subject. The ancients elevated the condition to the dignity of a definite disease entity, *morbus ructuosus*. It was not until after the studies of Van Helmont (1652) and near the end of the eighteenth century that the indefinite notion of morbus was abandoned. Interest then centered on the actual composition and origin of the gases themselves. Magendie (1813) gave the first clear account of air swallowing in his report of the case of a conscript who practiced auto-inflation in order to avoid military service. Chevillot (1833) made careful quantitative studies on the gases of man in health and disease. After 1865, German investigators expanded their studies until the whole subject of gastric fermentation and putrefaction was covered, not only from its chemical aspect, but from the bacteriologic and general clinical point of view as well (Naunyn, Hoppe-Seyler, Boas, and others). The more normal behavior and source of gastric gases was studied by Planer, Yllpö, and others, the general trend of whose work was toward the belief that the basis of gastric gases under normal conditions is constituted by atmospheric air, modified, however, by certain definite processes.

Magendie had pointed out that air swallowing was akin to the "cribbing" of horses, that the condition was by no means a rare one, and that it could be acquired by practice. He taught students to do it and made the first attempt to describe the mechanism of the act.

In spite of this work it was never fully realized that air swallowing is a perfectly normal physiologic process, and one that under pathologic conditions may give rise to disturbances that are generally assumed to be due to gases originating from the body. Quincke (1899) and later Bouveret gave complete expression to this viewpoint, and the latter suggested the term "aerophagia," which has been generally adopted. Much later work has followed. That by Smith and Le Wald[25] covering the condition in infants was reviewed two years ago.

Kantor considers briefly the composition of the gas found in the stomach of the adult, and the entry of air into the stomach. Air enters the stomach in one of two ways: It may either be carried down with fluids or solids in ordinary swallowing, or it may be "gulped" down alone. Both methods are carefully studied with the help of the fluoroscope.

Modern investigation has shown that in the act of swallowing "we are dealing with an orderly progression of pressures and inhibi-

tions which may be presented as far as they are known, schematically, as follows: A. Pressures: (1) initial buccopharyngeal thrust (Meltzer and collaborators); (2) esophageal peristalsis (Magendie, etc.). B. Inhibition: (1) inhibition of esophagus mouth (Killian); (2) relaxation of esophagus (Schreiber); (3) inhibition of cardia (Meltzer); (4) receptive relaxation of stomach (Cannon). This brings into greater prominence the part played by the cardia. The act is divided into three periods, instead of the classic two, and these three periods are the buccopharyngeal, the esophageal, and the cardiogastric.

Kantor describes in detail the act of air swallowing, which he practices himself, and has taught to others. In general it is much easier to swallow air in the recumbent than in the standing position.

The greater part of the air introduced into the stomach escapes through the esophagus by eructation. Closer observation shows that a very large number of people eructate. Kelling has found that in adults belching occurs whenever the intragastric tension reaches 25 cm. of water. Gastric tension is low at the time of swallowing and rises (Dobrovici) as digestion progresses. Individual sensitiveness to the presence of gas in the stomach, posture, gastric acidity, and peripheral reflexes all play a part. Aerophagia may be associated with eructation, and all persistent belchers should be regarded clinically as air-swallowers.

Air remaining in the stomach increases in bulk (as much as 12 per cent. in winter) through expansion due to the greater internal temperature. Its bulk diminishes in the digesting stomach owing to the absorption of oxygen—approximately 12 c.c. per minute (Yllpö). Air swallowed on an empty stomach may pass the pylorus, as shown by the fluoroscope.

De Buys and Henriques[62] report the result of some fluoroscopic examinations of the child's stomach, showing the effect of body posture in its position and emptying time. Active peristalsis in the stomach was noted in their youngest patient, aged 4 months. In one of their cases the adult type of stomach was reached at 3 years. The position of the stomach and especially the position of the solid contents of the stomach was found to be influenced by body posture. Motility of the stomach is most rapid in the right lateral position. The supine position produces a comparatively slow motility.

(To be continued)

62. De Buys, L. R., and Henriques, A.: Effect of Body Posture on Position and Emptying Time of Stomach. Am. Jour. Dis. Child., 1918, **15**, 190.

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